```
FILE 'REGISTRY' ENTERED AT 12:19:56 ON 03 FEB 2004

=> S EPOXIDE HYDROLASE/CN
L1            1 EPOXIDE HYDROLASE/CN

=> D

L1   ANSWER 1 OF 1  REGISTRY  COPYRIGHT 2004 ACS on STN
RN   9048-63-9  REGISTRY
CN   Hydratase, epoxide (9CI)  (CA INDEX NAME)
OTHER NAMES:
CN   cis-Epoxide hydrolase
CN   E.C. 3.3.2.3
CN   E.C. 4.2.1.63
CN   Epoxide hydrase
CN   Epoxide hydratase
CN     ***Epoxide hydrolase***
CN   Epoxide lyase
CN   Epoxyhydrolase
CN   Styrene oxide hydrolase
CN   trans-Stilbene oxide hydrolase
CN   Xenobiotic epoxide hydrolase
MF   Unspecified
CI   MAN
LC   STN Files:   ADISNEWS, AGRICOLA, ANABSTR, BIOBUSINESS, BIOSIS, BIOTECHNO,
       CA, CAPLUS, CASREACT, CEN, CHEMCATS, CHEMINFORMRX, CIN, EMBASE,
       NAPRALERT, NIOSHTIC, PROMT, TOXCENTER, USPAT2, USPATFULL

*** STRUCTURE DIAGRAM IS NOT AVAILABLE ***
            2291 REFERENCES IN FILE CA (1907 TO DATE)
               9 REFERENCES TO NON-SPECIFIC DERIVATIVES IN FILE CA
            2295 REFERENCES IN FILE CAPLUS (1907 TO DATE)


FILE 'CAPLUS' ENTERED AT 12:20:26 ON 03 FEB 2004

=> S EPOXIDE HYDROLASE;S L1 OR L2
         43287 EPOXIDE
         24681 EPOXIDES
         56279 EPOXIDE
                 (EPOXIDE OR EPOXIDES)
         17814 HYDROLASE
          7852 HYDROLASES
         21915 HYDROLASE
                 (HYDROLASE OR HYDROLASES)
L2        2211 EPOXIDE HYDROLASE
                 (EPOXIDE(W)HYDROLASE)


          2295 L1
L3        2804 L1 OR L2

=> S APERGILLUS;S FUNGUS OR FUNGAL
L4          40 APERGILLUS


         42146 FUNGUS
            17 FUNGUSES
         63087 FUNGI
             6 FUNGIS
         92987 FUNGUS
                 (FUNGUS OR FUNGUSES OR FUNGI OR FUNGIS)
         40071 FUNGAL
             7 FUNGALS
         40075 FUNGAL
                 (FUNGAL OR FUNGALS)
L5      113911 FUNGUS OR FUNGAL

=> S L4 AND L2
L6            0 L4 AND L2
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=> S L4 AND L3;S L5 AND L3
L7 0 L4 AND L3

L8 56 L5 AND L3

=> S ASPERGILLUS
43387 ASPERGILLUS
544 ASPERGILLI
104 ASPERGILLIS
L9 43482 ASPERGILLUS
(ASPERGILLUS OR ASPERGILLI OR ASPERGILLIS)

=> S L9 AND L3
L10 43 L9 AND L3

=> S L8 NOT L10
L11 35 L8 NOT L10

=> D L10 1-43 CBIB ABS

L10 ANSWER 1 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
2003:1013025 Enzymatic transformations. Part 55: Highly productive ***epoxide*** ***hydrolase*** catalyzed resolution of an azole antifungal key synthon. Monfort, Nicolas; Archelas, Alain; Furstoss, Roland (UMR CNRS 6111, Faculte des Sciences de Luminy, Groupe Biocatalyse et Chimie Fine, Universite de la Mediterranee, Marseille, 13288, Fr.). Tetrahedron, 60(3), 601-605 (English) 2004. CODEN: TETRAB. ISSN: 0040-4020. Publisher: Elsevier Science B.V..
AB A highly productive bioprocess for the prepn. of enantiopure azole antifungal chirons is described. These are key building blocks for the synthesis of new triazole drug derivs. known to display valuable activity against such infections as for instance fluconazole-resistant oro-oesophageal candidiasis. Using com. available recombinant ***Aspergillus*** niger ***epoxide*** ***hydrolase*** under optimized exptl. conditions, the hydrolytic kinetic resoln. of 1-chloro-2-(2,4-difluorophenyl)-2,3-epoxypropane was performed in plain water, at room temp., using a two-phase reactor. This methodol. allowed the process to be run at a substrate concn. as high as 500 g/L (i.e., 2.5 M) and afforded the (unreacted) epoxide and the corresponding vicinal diol, both in nearly enantiopure form and quant. yield.

L10 ANSWER 2 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
2003:996280 Enhancing the Enantioselectivity of an ***Epoxide*** ***Hydrolase*** by Directed Evolution. Reetz, Manfred T.; Torre, Claudia; Eipper, Andreas; Lohmer, Renate; Hermes, Marcus; Brunner, Birgit; Maichele, Andrea; Bocola, Marco; Arand, Michael; Cronin, Annette; Genzel, Yvonne; Archelas, Alain; Furstoss, Roland (Max-Planck-Institut fuer Kohlenforschung, Muelheim/Ruhr, 45470, Germany). Organic Letters, 6(2), 177-180 (English) 2004. CODEN: ORLEF7. ISSN: 1523-7060. Publisher: American Chemical Society.
AB The ***epoxide*** ***hydrolase*** (EH) from ***Aspergillus*** niger, which shows a selectivity factor of only E = 4.6 in the hydrolytic kinetic resoln. of glycidyl Ph ether, has been subjected to directed evolution for the purpose of enhancing enantioselectivity. After only one round of error-prone polymerase chain reaction (epPCR), enantioselectivity was more than doubled (E = 10.8). The improved mutant enzyme contains three amino acid exchanges, two of which are spatially far from the catalytically active center.

L10 ANSWER 3 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
2003:989603 Directed Evolution of the ***Epoxide*** ***Hydrolase*** from ***Aspergillus*** niger. Cedrone, Frederic; Niel, Sebastien; Roca, Sanja; Bhatnagar, Tej; Ait-Abdelkader, Nadra; Torre, Claudia; Krumm, Holger; Maichele, Andrea; Reetz, Manfred T.; Baratti, Jacques C. (Faculte des Sciences de Luminy UMR CNRS 6111 Case 901, 163 avenue de Luminy, 13288). Biocatalysis and Biotransformation, 21(6), 357-364 (English) 2003. CODEN: BOBOEQ. ISSN: 1024-2422. Publisher: Taylor & Francis Ltd..
AB An efficient and genetically stable expression system for the directed evolution of ***epoxide*** ***hydrolase*** from ***Aspergillus*** niger (ANEH) has been constructed. Error prone

polymerase chain reaction (PCR) with defined mutation rates was used to create biodiversity in two libraries of mutants. Screening for activity allowed the isolation of clones with improved properties. One of these clones shows an expression level 3.4 higher than the original wild type clone in E. coli SG13009 and a 3.3 fold increased catalytic efficiency on 4-(p-nitrophenoxy)-1,2-epoxybutane. In addn., a screening assay for detg. the enantioselectivity in the kinetic resoln. of styrene oxide has been established using mass spectrometry.

L10 ANSWER 4 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
2003:573708 Document No. 139:306570 Enzymatic transformations. Immobilized A. niger ***epoxide*** ***hydrolase*** as a novel biocatalytic tool for repeated-batch hydrolytic kinetic resolution of epoxides. Mateo, Cesar; Archelas, Alain; Fernandez-Lafuente, Roberto; Guisan, Jose Manuel; Furstoss, Roland (Groupe Biocatalyse et Chimie Fine, UMR CNRS 6111, Universite de la Mediterranee, Marseille, 13288, Fr.). Organic & Biomolecular Chemistry, 1(15), 2739-2743 (English) 2003. CODEN: OBCRAK. ISSN: 1477-0520. Publisher: Royal Society of Chemistry.
AB Studies aimed at immobilization of the ***Aspergillus*** niger ***epoxide*** ***hydrolase*** were performed. The use of conventional approaches, i.e. of com. available supports and classical methodologies, only led to low stabilization and unsatisfactory enzymic activity recovery. Therefore, a new strategy based on the use of a "second generation" type of epoxy-activated supports allowing multi-point covalent immobilization, i.e. Eupergit C, partially modified with ethylene diamine (Eupergit C/EDA), and of an adequate exptl. procedure was set up. This allowed us to prep. an immobilized biocatalyst with 70% retention of the initial enzymic activity and a stabilization factor of about 30. Interestingly, this biocatalyst also led to a noticeable increase of the E value for the resoln. of two test substrates, styrene oxide and p-chlorostyrene oxide. This was improved from about 25 to 56 and from 40 to 100, resp. A typical repeated batch expt. indicated that the thus immobilized enzyme could be re-used for over 12 cycles without any noticeable loss of enzymic activity or change in enantioselectivity. This therefore opens the way for the use of an heterogeneous catalysis' methodol. for achieving the prepn. of various enantiopure epoxides via biocatalyzed hydrolytic kinetic resoln.

L10 ANSWER 5 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
2003:571327 Document No. 139:213000 Method for preparing chiral aryloxirane derivatives and its diol by selective resolution with ***Aspergillus*** niger. Jin, Hao; Li, Zuyi (Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, Peop. Rep. China). Faming Zhuanli Shenqing Gongkai Shuomingshu CN 1369565 A 20020918, 30 pp. (Chinese). CODEN: CNXXEV. APPLICATION: CN 2002-110718 20020131.
AB (S)-R1R2Ar-oxirane and its (R)-diol derivs. (Ar = Ph, naphthalenyl, or pyridyl and R1 and/or R2 = H, C1- 4 alkyl, NO2, CN, CF3, or halo) are prepd. by asym. hydrolysis of 0.1-20 g L-1 aryloxirane derivs. with ***epoxide*** ***hydrolase*** -producing ***Aspergillus*** niger CGMCC0,496 as catalyst at 20-35.degree. in 0.01-0.3M phosphate buffer (pH 5.0-9.0)-DMF for 0.2-3 h. The optically active oxirane derivs. and chiral diols thus prepd. are useful for manufg. drugs for control of cardiovascular and lung disorders.

L10 ANSWER 6 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
2003:190753 Document No. 139:2702 A spectrophotometric assay for measuring and detecting an ***epoxide*** ***hydrolase*** activity. Mateo, Cesar; Archelas, Alain; Furstoss, Roland (Faculte des Sciences de Luminy, UMR CNRS 6111, Universite de la Mediterranee, Marseille, 13288, Fr.). Analytical Biochemistry, 314(1), 135-141 (English) 2003. CODEN: ANBCA2. ISSN: 0003-2697. Publisher: Elsevier Science.
AB The development of a novel and simple spectrophotometric assay which allows one to achieve the continuous, rapid, sensitive, and accurate detn. of ***epoxide*** ***hydrolase*** (I) activity is reported. This assay is based on the elaboration of a coupled enzymic/chem. methodol. which allows quantification of I activity within 3 min, and offers good sensitivity of .apprx.10 .mu.M min-1. Thus, an arom. epoxide such as styrene oxide is hydrolyzed by I to 1-phenyl-1,2-ethanediol, which in turn is oxidized to benzaldehyde by Na metaperiodate; the benzaldehyde formed can be visualized at very low levels at 290 nm thanks to its very strong UV absorbancy (.epsilon. = 1356 M-1 cm-1). I activity can therefore be

detd. continuously, with great sensitivity and accuracy, simply by measuring, at very low conversion ratio, the increase in UV absorbancy. The applicability of this test for the detn. of ***Aspergillus*** niger I activity with some other arom. epoxides was shown and some limitations were also explored. This assay should be particularly useful for different applications, e.g., (1) activity localization during purifn. of such enzymes, (2) very rapid detn. of kinetic consts., and (3) high-throughput screening expts.

L10 ANSWER 7 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN

2003:6148 Document No. 138:54642 Methods for the manufacture of pure single enantiomer compounds and for selecting enantioselective enzymes. Weiner, David; Hitchman, Tim; Zhao, Lishan; Burk, Mark (Diversa Corporation, USA). PCT Int. Appl. WO 2003000909 A2 20030103, 122 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, BZ, CA, CH, CN, CO, CR, CU, CZ, DE, DK, DM, DZ, EC, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, MZ, NO, NZ, OM, PH, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TN, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZM, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG, TR. (English). CODEN: PIXXD2. APPLICATION: WO 2002-US19706 20020621. PRIORITY: US 2001-PV300189 20010621; US 2001-PV340291 20011214.

AB The invention provides biocatalytic methods for the manuf. of pure single enantiomer compds. The invention provides methods of screening for enzymes which are highly enantioselective or enzymes that can provide any desired stereoisomer of a compd. The invention provides the use of single enantiomer substrates in performing a growth screen of a clonal library to identify highly stereoselective enzymes. In one aspect, methods for screening and identification of enzymes, e.g., transaminases, nitrilases, aldolases, ***epoxide*** ***hydrolases*** are provided. Methods for the prodn. and screening of gene libraries generated form nucleic acids isolated from more than one organism for enzyme, e.g., transaminase, activities are also provided.

L10 ANSWER 8 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN

2002:878731 Document No. 138:287445 Enzymatic transformations. Part 53: ***Epoxide*** ***hydrolase*** -catalyzed resolution of key synthons for azole antifungal agents. Monfort, Nicolas; Archelas, Alain; Furstoss, Roland (Faculte des Sciences de Luminy, Groupe Biocatalyse et Chimie Fine, Universite de la Mediterranee, UMR CNRS 6111, Marseille, 13288, Fr.). Tetrahedron: Asymmetry, 13(22), 2399-2401 (English) 2002. CODEN: TASYE3. ISSN: 0957-4166. OTHER SOURCES: CASREACT 138:287445. Publisher: Elsevier Science Ltd..

AB The biocatalyzed hydrolytic kinetic resoln. (BHKR) of a key building block allowing the synthesis of an enantiopure azole antifungal compd. is described. This is based on the ***epoxide*** ***hydrolase*** -catalyzed resoln. of a racemic epoxide. Using ***epoxide*** ***hydrolase*** from ***Aspergillus*** niger, both the unreacted epoxide and the formed diol were obtained with excellent yield and very high ee (>98%). Interestingly, both products can be used for the synthesis of the target mol., thus allowing the theor. 50% yield limitation linked to such resoln. processes to be overcome.

L10 ANSWER 9 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN

2002:796311 Document No. 138:165574 Cloning, characterization and heterologous expression of ***epoxide*** ***hydrolase*** -encoding cDNA sequences from yeasts belonging to the genera Rhodotorula and Rhodosporidium. Visser, Hans; Weijers, Carel A. G. M.; van Ooyen, Albert J. J.; Verdoes, Jan C. (Division of Industrial Microbiology, Wageningen University, Wageningen, 6703 HD, Neth.). Biotechnology Letters, 24(20), 1687-1694 (English) 2002. CODEN: BILED3. ISSN: 0141-5492. Publisher: Kluwer Academic Publishers.

AB ***Epoxide*** ***hydrolase*** -encoding cDNA sequences were isolated from the basidiomycetous yeast species Rhodosporidium toruloides CBS 349, Rhodosporidium toruloides CBS 14 and Rhodotorula araucariae CBS 6031 in order to evaluate the mol. data and potential application of this type of enzymes. The deduced amino acid sequences were similar to those of the known ***epoxide*** ***hydrolases*** from Rhodotorula glutinis CBS 8761, Xanthophyllomyces dendrorhous CBS 6938 and

· ***Aspergillus*** niger LCP 521, which all correspond to the group of the microsomal ***epoxide*** ***hydrolases*** . The ***epoxide*** ***hydrolase*** encoding cDNAs of the Rhodosporidium and Rhodotorula species were expressed in Escherichia coli. The recombinant strains were able to hydrolyze trans-1-phenyl-1,2-epoxypropane with high enantioselectivity.

L10 ANSWER 10 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
2002:288776 Document No. 137:2260 The adrenaline test for enzymes. Wahler, Denis; Reymond, Jean-Louis (Department of Chemistry & Biochemistry, University of Bern, Bern, 3012, Switz.). Angewandte Chemie, International Edition, 41(7), 1229-1232 (English) 2002. CODEN: ACIEF5. ISSN: 1433-7851. Publisher: Wiley-VCH Verlag GmbH.
AB A versatile high-throughput enzyme assay is demonstrated which is based on the colorimetric back-titrn. of sodium periodate with L-adrenaline. Enzyme activity is assocd. with the depletion of sodium periodate by the reaction product (P), and indicated by the decrease in the amt. of the red dye adrenochrome produced by the oxidn. of adrenaline by sodium periodate. The assay quantitates vicinal diols, amino alcs., diamines and .alpha.-hydroxy ketones. The assay was applied to measure lipases, esterases, phytases and ***epoxide*** ***hydrolases*** . The versatility of the assay in terms of substrate structures was demonstrated for the ***epoxide*** ***hydrolases*** from ***Aspergillus*** niger and Rhodotorula glutinis.

L10 ANSWER 11 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
2002:190585 ***Epoxide*** ***hydrolase*** -catalyzed asymmetric resolution for the production of chiral styrene oxide. Lee, Eun-Yeol; Lee, Eun J.; Kim, Hyun S.; Kim, Choi H.; Park, Won H.; Kim, Hee S.; Lee, Jong-Chan; Lee, Ji W.; You, Seung S. (Department of Food Science and Technology, Kyungsung University, Pusan, 608-736, S. Korea). Abstracts of Papers, 223rd ACS National Meeting, Orlando, FL, United States, April 7-11, 2002, ORGN-050. American Chemical Society: Washington, D. C. (English) 2002. CODEN: 69CKQP.
AB A newly isolated ***Aspergillus*** niger possessing the novel ***epoxide*** ***hydrolase*** (EHase) activity was investigated for the enantioselective hydrolysis of racemic arom. epoxides. The gene encoding EHase was cloned by RT-PCR, and mol. characteristics of the EHase gene were compared with other microbial EHases. The cloned gene encodes 398 amino acids with a deduced mol. mass of 44.5 kDa and pI of 4.83, and sequence homol. with other microbial EHase was low. Functional recombinant EHase could be obtained by heterologous expressions in E. coli and yeast. Enantioselectivity of recombinant EHase was tested for valuable arom. epoxide intermediates. Reaction conditions of EHase-catalyzed asym. resoln. were optimized for the prodn. of chiral styrene oxide.

L10 ANSWER 12 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
2002:66574 Document No. 136:308605 Microbiological transformations 50: selection of ***epoxide*** ***hydrolases*** for enzymatic resolution of 2-, 3- or 4-pyridyloxirane. Genzel, Yvonne; Archelas, Alain; Broxterman, Q. B.; Schulze, Birgit; Furstoss, Roland (Faculte des Sciences de Luminy, Groupe Biocatalyse et Chimie Fine, UMR CNRS 6111, Universite de la Mediterranee, Marseille, 13288, Fr.). Journal of Molecular Catalysis B: Enzymatic, 16(5-6), 217-222 (English) 2002. CODEN: JMCEF8. ISSN: 1381-1177. Publisher: Elsevier Science B.V..
AB A study aimed to select efficient ***epoxide*** ***hydrolases*** (EHs) allowing to achieve the enzymic resoln. of 2-, 3- and 4-pyridyloxirane (1-3) has been achieved, using 2-pyridyloxirane (1) as test substrate. Five thus selected EH-sources that showed interesting enantioselectivity were looked at in more detail for the conversion of 1-3.

L10 ANSWER 13 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
2002:3675 Document No. 136:337488 Isolation and fermentation condition of ***Aspergillus*** niger capable of production epoxide hydrolysas. Sha, Qian; Yang, Liu; Wang, Jianjun; Zheng, Guojun; Wu, Jin; Sun, Wanru (State Key Laboratory of Microbiology Resources, Institute of Microbiology, Chinese Academy of Sciences, Beijing, 100080, Peop. Rep. China). Junwu Xitong, 20(4), 494-502 (Chinese) 2001. CODEN: JUXIFB. ISSN: 1007-3515. Publisher: Kexue Chubanshe.

AB · ***Aspergillus*** niger SQ-6 producing ***epoxide*** ***hydrolase*** was isolated from 60 soil samples using Ph epoxy ethane as a sole carbon source. Conditions for enzyme prodn. were investigated. It found that the synthesis of the enzyme did not need inductor and high enzyme activity was achieved when 2.0% corn ext. and 2.0% sucrose were used as carbon and nitrogen sources, resp., at optical temp. 37.degree.. The cells of ***Aspergillus*** niger QS-6 were used for stereoselective conversion of Ph epoxy ethane to phenylglycol. About 41% of conversion yield and 99% ee value of product were obtained.

L10 ANSWER 14 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
2001:856783 Document No. 136:228659 A spectrophotometric method to assay ***epoxide*** ***hydrolase*** activity. Bhatnagar, Tej; Manoj, Kelath M.; Baratti, Jacques C. (Biocatalyse et Chimie Fine, Universite de la Mediterranee, Faculte des Sciences de Luminy, Marseille, 13288, Fr.). Journal of Biochemical and Biophysical Methods, 50(1), 1-13 (English) 2001. CODEN: JBBMDG. ISSN: 0165-022X. Publisher: Elsevier Science Ireland Ltd..
AB The ***Aspergillus*** niger ***epoxide*** ***hydrolase*** activity was assayed by spectrophotometric using (rac) p-nitrostryrene oxide (pNSO) as substrate. Both the substrate (pNSO) and the reaction product, p-nitrostryrene diol (pNSD), had a strong absorbance in UV at 280 nm. The assay was based on the measure of the pNSD absorbance of the water phase after extn. of the non-reacted pNSO with a solvent. Among the five solvents tested, chloroform was selected since it extd. more than 99% of the epoxide and only 32% of the produced diol. This extn. yield was independent of the diol and epoxide concns. and it was fairly reproducible. Using different enzyme amts., the reaction kinetics were linear for the first 10 min corresponding to degrees of conversion less than 5% for the epoxide. Two controls were run simultaneously, one with the substrate alone (epoxide hydrolysis and non-complete extn.) and one with the enzyme alone (enzyme absorbance at 280 nm). The resulting .DELTA.OD/min was linear with the amt. of enzyme added within a large range from 2 to 80 .mu.g of the EH prepn. The new spectrophotometric assay correlates well with the previous HPLC assay and could be used routinely for an easy and fast evaluation of EH activity. The kinetic parameters of (rac) pNSO hydrolysis by A. niger ***epoxide*** ***hydrolase*** could be easily detd. and Km (1.1 mM) compared well with that previously reported (1.0 mM).

L10 ANSWER 15 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
2001:790724 Document No. 136:66185 Immobilization of the ***epoxide*** ***hydrolase*** from ***Aspergillus*** niger. Karboune, S.; Amourache, L.; Nellaiah, H.; Morisseau, C.; Baratti, J. (Universite de la Mediterranee, Biocatalyse et Chimie Fine, CNRS UMR 6111, Faculte des Sciences de Luminy, Marseille, 13288, Fr.). Biotechnology Letters, 23(19), 1633-1639 (English) 2001. CODEN: BILED3. ISSN: 0141-5492. Publisher: Kluwer Academic Publishers.
AB Three methods for the immobilization of the ***epoxide*** ***hydrolase*** from the fungus ***Aspergillus*** niger were tested. The highest immobilization yield (90%) and retention of activity (65%) were obtained by adsorption onto DEAE-cellulose compared to adsorption onto hydrophobic porous polypropylene and covalent linkage using Eupergit resin. The enzymic properties of the immobilized enzyme were similar to those of the free enzyme with respect to the effect of temp. and pH on both activity and stability as well as the effect of solvent (DMF) on activity. The kinetic parameters were affected leading to lower KM(app) and higher Vm(app).

L10 ANSWER 16 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
2001:749456 Document No. 135:256196 ***Aspergillus*** niger strain and its culture method and application. Li, Zuyi; Jin, Hao (Shanghai Inst. of Organic Chemistry, Chinese Academy of Sciences, Peop. Rep. China). Faming Zhuanli Shenqing Gongkai Shuomingshu CN 1291647 A 20010418, 9 pp. (Chinese). CODEN: CNXXEV. APPLICATION: CN 2000-127451 20001117.
AB The ***epoxide*** ***hydrolase*** -producing ***Aspergillus*** niger 5450 (CGMCC No.0496) is prepd. by culturing in culture medium at 10-35.degree. for 2-3 d, fermenting in culture liq. at 10-35.degree. for 2-3 d, collecting mycelium, washing with 0.8% NaCl soln., and centrifugating or filtering. The culture medium or liq. comprises C source 10-30, N source 6-15, agar 1-3, K2HPO4 H2O 1.0, KCl 0.5, MgSO4 H2O

0.5, and FeSO4 H2O 0.01 g L-1, and its pH is 3.0-7.0. The N source is selected from corn slurry, yeast ext., or corn meal, preferably corn meal. The C source is selected from fructose, glucose, or sucrose, preferably fructose. The ***Aspergillus*** niger strain is used as catalyst for asym. synthesis of chiral epoxides or 1,2-diol compds.

L10 ANSWER 17 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
2001:182773 Document No. 134:353215 Biocatalytic resolution of para-nitrostyrene oxide by resting cells of different ***Aspergillus*** niger strains. Jin, Hao; Wang, Qing; Li, Zu-Yi (State Key Laboratory of Bio-organic & Natural Products Chemistry, Shanghai Institute of Organic Chemistry, Chinese Academy of Sciences, Shanghai, 200032, Peop. Rep. China). Chinese Journal of Chemistry, 19(3), 272-275 (English) 2001. CODEN: CJOCEV. ISSN: 1001-604X. OTHER SOURCES: CASREACT 134:353215. Publisher: Science Press.
AB Biocatalytic resoln. of racemic p-nitrostyrene oxide was accomplished by employing the ***epoxide*** ***hydrolases*** from the whole cells of several A. niger strains. In the cases investigated, excellent selectivity was achieved with such strains as A. niger 5450, A. niger 5320.

L10 ANSWER 18 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
2000:901197 Document No. 134:222570 Microbiological transformations. 47. A step toward a green chemistry preparation of enantiopure (S)-2-, -3-, and -4-pyridyloxirane via an ***epoxide*** ***hydrolase*** catalyzed kinetic resolution. Genzel, Yvonne; Archelas, Alain; Broxterman, Q. B.; Schulze, Birgit; Furstoss, Roland (Groupe Biocatalyse et Chimie Fine, ESA 6111 Associee au CNRS Universite de la Mediterranee Faculte des Sciences de Luminy, Marseille, 13288, Fr.). Journal of Organic Chemistry, 66(2), 538-543 (English) 2001. CODEN: JOCEAH. ISSN: 0022-3263. OTHER SOURCES: CASREACT 134:222570. Publisher: American Chemical Society.
AB The biocatalyzed hydrolytic kinetic resoln. of 2-, 3-, and 4-pyridyloxirane by the ***Aspergillus*** niger ***epoxide*** ***hydrolase*** (EH) has been explored. This was used to perform a gram scale prepn. of these epoxides of (S) abs. configuration using a process performed at a concn. as high as 10 g/L (82 mM). All three epoxides have been obtained in a nearly enantiopure form (ee > 98%). Interestingly, it was shown that this biotransformation could be achieved using plain water instead of buffer soln., an important improvement as far as downstream processing of an eventual industrial process is concerned. Neither of these substrates could be obtained in reasonable enantiomeric purity and yield using the nowadays most efficient metal-based catalysts.

L10 ANSWER 19 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
2000:814634 Document No. 133:360460 ***Aspergillus*** ***epoxide*** ***hydrolase*** and cDNA and method for preparing chiral epoxides and diols. Arand, Michael; Archelas, Alain Robert; Baratti, Jacques; Furstoss, Roland (Centre National de la Recherche Scientifique, Fr.). PCT Int. Appl. WO 2000068394 A1 20001116, 43 pp. DESIGNATED STATES: W: AE, AG, AL, AM, AT, AU, AZ, BA, BB, BG, BR, BY, CA, CH, CN, CR, CU, CZ, DE, DK, DM, DZ, EE, ES, FI, GB, GD, GE, GH, GM, HR, HU, ID, IL, IN, IS, JP, KE, KG, KP, KR, KZ, LC, LK, LR, LS, LT, LU, LV, MA, MD, MG, MK, MN, MW, MX, NO, NZ, PL, PT, RO, RU, SD, SE, SG, SI, SK, SL, TJ, TM, TR, TT, TZ, UA, UG, US, UZ, VN, YU, ZA, ZW, AM, AZ, BY, KG, KZ, MD, RU, TJ, TM; RW: AT, BE, BF, BJ, CF, CG, CH, CI, CM, CY, DE, DK, ES, FI, FR, GA, GB, GR, IE, IT, LU, MC, ML, MR, NE, NL, PT, SE, SN, TD, TG. (French). CODEN: PIXXD2. APPLICATION: WO 2000-FR1217 20000505. PRIORITY: FR 1999-5711 19990505.
AB The invention concerns proteins of fungal origin having an ***epoxide*** ***hydrolase*** activity, such as those obtained in essentially pure form by extn. from fungi cells, or by culturing in host cells transformed by a nucleotide sequence coding for said fungal proteins. The invention also concerns the uses thereof, in particular for implementing methods for prepg. enantiopure epoxides and/or diols. Thus, the ***epoxide*** ***hydrolase*** of A. niger was purified. The enzyme is a tetramer of four identical 45-kilodalton subunits. It has a pI of 4.5 and optimum activity at pH 7 and 40.degree.. Expts. with inhibitors indicated that cysteine(s) is important for enzymic activity and that histidine(s) participates in the catalytic mechanism. Using p-nitrostyrene oxide as substrate, the R-enantiomer was found to have a higher affinity for the enzyme, and to be hydrolyzed faster, than the S-enantiomer. The cDNA for

this enzyme was cloned and sequenced.

L10 ANSWER 20 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
2000:656710 Document No. 134:4821 Microbiological transformations. Part 46: Preparation of enantiopure (S)-2-pyridyloxirane via ***epoxide*** ***hydrolase*** -catalyzed kinetic resolution. Genzel, Y.; Archelas, A.; Broxterman, Q. B.; Schulze, B.; Furstoss, R. (Faculte de Sciences de Luminy, Groupe Biocatalyse et Chimie Fine, ESA 6111 Associee au CNRS, Universite de la Mediterranee, Marseille, 13288, Fr.). Tetrahedron: Asymmetry, 11(15), 3041-3044 (English) 2000. CODEN: TASYE3. ISSN: 0957-4166. OTHER SOURCES: CASREACT 134:4821. Publisher: Elsevier Science Ltd..
AB The hydrolytic kinetic resoln. (HKR) of 2-pyridyloxirane is described, using the overexpressed ***epoxide*** ***hydrolase*** from the filamentous fungus ***Aspergillus*** niger. This allows the prepn. of the (S)-enantiomer of this product in enantiopure form (ee > 99%), which could not be obtained using conventional chem. methods.

L10 ANSWER 21 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
2000:441464 Document No. 133:55322 ***Epoxide*** ***hydrolase*** mutant with improved stereoselectivity. Rink, Rick; Lutjes, Spelberg Jeffrey Harald; Nardini, Marco; Dijkstra, Bauke Wiepke; Kellogg, Richard Morrisen; Janssen, Dirk Barend (DSM N.V., Neth.). Eur. Pat. Appl. EP 1013768 A1 20000628, 11 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO. (English). CODEN: EPXXDW. APPLICATION: EP 1998-204315 19981218.
AB Mutant ***epoxide*** ***hydrolases*** are provided having an amino acid substitution of a tyrosine residue in the cap domain of the wild-type ***epoxide*** ***hydrolase*** , in particular mutant ***epoxide*** ***hydrolases*** having an amino acid substitution of the tyrosine residue corresponding to Tyr152 or Tyr215 with Phe in the ***epoxide*** ***hydrolase*** from Agrobacterium radiobacter AD1. The Tyr residues in the cap domain of ***epoxide*** ***hydrolases*** are involved in the catalytic mechanism and det. the stereoselectivity. Thus, the action of Tyr215Phe ***epoxide*** ***hydrolase*** from A. radiobacter with styrene oxide substrates results in higher enantiomeric excess and yield than does the wild-type enzyme. The invention also relates to nucleic acid sequences encoding such mutant ***epoxide*** ***hydrolases*** expression constructs wherein such nucleic acid sequence according is operably linked to a regulatory region capable of directing the expression of the mutant ***epoxide*** ***hydrolase*** in a suitable expression host, vectors capable of transforming a host cell characterized in that the vector contg. such expression construct, and transformed host cells transformed with such a vector. Such mutant ***epoxide*** ***hydrolases*** may be used for the prepn. of optically active epoxides and/or diols.

L10 ANSWER 22 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
2000:148366 Document No. 132:177414 Structure of ***Aspergillus*** niger ***epoxide*** ***hydrolase*** at 1.8 .ANG. resolution: implications for the structure and function of the mammalian microsomal class of ***epoxide*** ***hydrolases*** . Zou, Jinyu; Hallberg, B. Martin; Bergfors, Terese; Oesch, Franz; Arand, Michael; Mowbray, Sherry L.; Jones, T. Alwyn (Department of Cell and Molecular Biology, Uppsala University, BMC, Uppsala, S-751 24, Swed.). Structure (London), 8(2), 111-122 (English) 2000. CODEN: STRUE6. ISSN: 0969-2126. Publisher: Elsevier Science Ltd..
AB ***Epoxide*** ***hydrolases*** play important roles in the defense of cells against potentially harmful epoxides. Conversion of epoxides into less toxic and more easily excreted diols is a universally successful strategy. A no. of microorganisms employ the same chem. to process epoxides for use as carbon sources. Here, the x-ray crystal structure of ***epoxide*** ***hydrolase*** from A. niger was detd. at 3.5 .ANG. resoln. using the multiwavelength anomalous dispersion (MAD) method, and then refined at 1.8 .ANG. resoln. There was a dimer consisting of 2 44-kDa subunits in the asym. unit. Each subunit consisted of an .alpha./.beta. hydrolase fold, and a primarily helical lid over the active site. The dimer interface included lid-lid interactions as well as contributions from an N-terminal meander. The active site contained a classical catalytic triad, and 2 Tyr and 1 Glu residues that were likely to assist in catalysis. The ***Aspergillus*** enzyme provides the 1st

structure of an ***epoxide*** ***hydrolase*** with strong relations to the most important enzyme of human epoxide metab., microsomal ***epoxide*** ***hydrolase*** . Differences in active site residues, esp. in components that assist in epoxide ring opening and hydrolysis of the enzyme-substrate intermediate, might explain why the fungal enzyme attains the greater speeds necessary for an effective metabolic enzyme. The N-terminal domain that is characteristic of microsomal ***epoxide*** ***hydrolases*** corresponded to a meander that is crit. for dimer formation in the ***Aspergillus*** enzyme.

L10 ANSWER 23 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
1999:768069 Document No. 132:104628 Cloning and molecular characterization of a soluble ***epoxide*** ***hydrolase*** from ***Aspergillus*** niger that is related to mammalian microsomal ***epoxide*** ***hydrolase*** . Arand, Michael; Hemmer, Heike; Durk, Heike; Baratti, Jacques; Archelas, Alain; Furstoss, Roland; Oesch, Franz (Institute of Toxicology, University of Mainz, Mainz, D-55131, Germany). Biochemical Journal, 344(1), 273-280 (English) 1999. CODEN: BIJOAK. ISSN: 0264-6021. Publisher: Portland Press Ltd..
AB ***Aspergillus*** niger strain LCP521 harbors a highly processive ***epoxide*** ***hydrolase*** (EH) that is of particular interest for the enantioselective bio-org. synthesis of fine chems. In the present work, we report the isolation of the gene and cDNA for this EH by use of inverse PCR. The gene is composed of nine exons, the first of which is apparently non-coding. The deduced protein of the A. niger EH shares significant sequence similarity with the mammalian microsomal EHs (mEH). In contrast to these, however, the protein from A. niger lacks the common N-terminal membrane anchor, in line with the fact that this enzyme is, indeed, sol. in its native environment. Recombinant expression of the isolated cDNA in Escherichia coli yielded a fully active EH with similar characteristics to the fungal enzyme. Sequence comparison with mammalian EHs suggested that Asp192, Asp348 and His374 constituted the catalytic triad of the fungal EH. This was subsequently substantiated by the anal. of resp. mutants constructed by site-directed mutagenesis. The presence of an aspartic acid residue in the charge-relay system of the A. niger enzyme, in contrast to a glutamic acid residue in the resp. position of all mEHs analyzed to date, may be one important contributor to the exceptionally high turnover no. of the fungal enzyme when compared with its mammalian relatives. Recombinant expression of the enzyme in E. coli offers a versatile tool for the bio-org. chemist for the chiral synthesis of a variety of fine chems.

L10 ANSWER 24 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
1999:503850 Document No. 131:296887 Purification and characterization of a highly enantioselective ***epoxide*** ***hydrolase*** from ***Aspergillus*** niger. Morisseau, Christophe; Archelas, Alain; Guitton, Carole; Faucher, Didier; Furstoss, Roland; Baratti, Jacques C. (Biocatalysis and Fine Chemistry Group, Universite de la Mediterranee, ESA CNRS 6111, Marseille, 13288, Fr.). European Journal of Biochemistry, 263(2), 386-395 (English) 1999. CODEN: EJBCAI. ISSN: 0014-2956. Publisher: Blackwell Science Ltd..
AB The ***epoxide*** ***hydrolase*** from ***Aspergillus*** niger was purified to homogeneity using a four-step procedure and p-nitrostyrene oxide (pNSO) as substrate. The enzyme was purified 246-fold with 4% activity yield. The protein is a tetramer composed of four identical subunits of mol. mass 45 kDa. Maximum activity was obsd. at 40.degree., pH 7.0, and with DMF as cosolvent to dissolve pNSO. Hydrolysis of pNSO was highly enantioselective, with an E value (i.e. enantiomeric ratio) of 40 and a high regioselectivity (97%) for the less hindered carbon atom of the epoxide. This enzyme may be a good biocatalyst for the prepn. of enantiopure epoxides or diols.

L10 ANSWER 25 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
1999:390837 Document No. 131:144366 Microbiological Transformations 43. ***Epoxide*** ***Hydrolases*** as Tools for the Synthesis of Enantiopure .alpha.-Methylstyrene Oxides: A New and Efficient Synthesis of (S)-Ibuprofen. Cleij, M.; Archelas, A.; Furstoss, R. (Groupe Biocatalyse et Chimie Fine ESA 6111 associee au CNRS, Faculte des Sciences de Luminy Universite de la Mediterranee, Marseille, 13288, Fr.). Journal of Organic Chemistry, 64(14), 5029-5035 (English) 1999. CODEN: JOCEAH. ISSN: 0022-3263. OTHER SOURCES: CASREACT 131:144366. Publisher: American

Chemical Society.
AB Biohydrolysis of various .alpha.-methylstyrene oxide derivs., differently substituted at the arom. ring, was investigated using 10 ***epoxide*** ***hydrolases*** from different origins. Our results indicate that the enantioselectivity of these biohydrolysis strongly depends on the nature of the enzyme and of the substituent. Using some of these enzymes, this approach allows to prep. these epoxides in high optical purity. The potentiality to perform efficient preparative-scale resoln. using such a biocatalyst was illustrated by the four-step synthesis of (S)-ibuprofen, a nonsteroidal antiinflammatory drug and household pain killer, one of the top-ten drugs sold worldwide. Using a combined chemoenzymic strategy, we were thus able to set up a four-step enantioconvergent procedure allowing for the synthesis of this compd. in optically pure form and with a 47% overall yield, including the resoln. process, due to a possible recycling of the formed diol via chem. racemization.

L10 ANSWER 26 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
1999:190773 Document No. 130:349529 First evaluation of the Brazilian microorganisms biocatalytic potential. Cagnon, J. R.; Porto, A. L. M.; Marsaioli, A. J.; Manfio, G. P.; Eguchi, S. Y. (Instituto de Quimica, UNICAMP, Campinas, CEP: 13083-970, Brazil). Chemosphere, 38(10), 2237-2242 (English) 1999. CODEN: CMSHAF. ISSN: 0045-6535. OTHER SOURCES: CASREACT 130:349529. Publisher: Elsevier Science Ltd..
AB The biocatalytic potential of 2 novel Brazilian strains of ***Aspergillus*** niger and Rhodotorula glutinis revealed enantioselective ***epoxide*** ***hydrolase*** activity in the asymmetrization of meso-epoxide and monosubstituted epoxides, resp. These 2 types of oxirane derivs. are not usually good substrates for biocatalytic enantioselective conversion.

L10 ANSWER 27 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
1999:123763 Document No. 130:293062 Stereoselectivities of microbial ***epoxide*** ***hydrolases*** . Orru, Romano V. A.; Faber, Kurt (Institute of Organic Chemistry, University of Graz, Graz, A-8010, Austria). Current Opinion in Chemical Biology, 3(1), 16-21 (English) 1999. CODEN: COCBF4. ISSN: 1367-5931. Publisher: Current Biology Publications.
AB A review with 30 refs. ***Epoxide*** ***hydrolases*** from bacterial and fungal sources are highly versatile biocatalysts for the asym. hydrolysis of epoxides on a preparative scale. Besides kinetic resoln., which yields the corresponding enantiomerically enriched vicinal diol and the remaining nonconverted epoxide, enantioconvergent processes are also possible, which lead to the formation of a single enantiomeric diol from a racemic oxirane. The data available to date indicate that the enantioselectivities of enzymes from certain microbial sources can be correlated to the substitutional pattern of various types of substrates: red yeasts (e.g. Rhodotorula or Rhodosporidium sp.) give best enantioselectivities with monosubstituted oxiranes; fungal cells (e.g. from ***Aspergillus*** and Beauveria sp.) are best suited for styrene oxide-type substrates; bacterial enzymes, on the other hand (in particular from Actinomycetes such as Rhodococcus and Nocardia sp.) are the biocatalysts of choice for more highly substituted 2,2- and 2,3-disubstituted epoxides.

L10 ANSWER 28 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
1999:6421 Document No. 130:196334 ***Epoxide*** ***hydrolases*** and their synthetic applications. Orru, Romano V. A.; Archelas, Alain; Furstoss, Roland; Faber, Kurt (Institute of Organic Chemistry, Graz University of Technology, Graz, A-8010, Austria). Advances in Biochemical Engineering/Biotechnology, 63(Biotransformations), 145-167 (English) 1999. CODEN: ABEBDZ. ISSN: 0724-6145. Publisher: Springer-Verlag.
AB Review with 103 refs. Chiral epoxides and 1,2-diols, which are central building blocks for the asym. synthesis of bioactive compds., can be obtained by using enzymes, i.e. ***epoxide*** ***hydrolases*** , which catalyze the enantioselective hydrolysis of epoxides. These biocatalysts have recently been found to be more widely distributed in fungi and bacteria than previously expected. Sufficient sources from bacteria, such as Rhodococcus and Nocardia spp., or fungi, such as ***Aspergillus*** and Beauveria spp., have now been identified. The reaction proceeds via an SN2-specific opening of the epoxide, leading to the formation of the corresponding trans-configured 1,2-diol. For the

resoln. of racemic monosubstituted and 2,2- or 2,3-disubstituted substrates, various fungi and bacteria have been shown to possess excellent enantioselectivities. Addnl., different methods, which lead to the formation of the optically pure product diol in a chem. yield far beyond the 50% mark (which is intrinsic to classic kinetic resolns.), are discussed. In addn., the use of non-natural nucleophiles such as azides or amines provides access to enantiomerically enriched vicinal azido- and amino-alcs. The synthetic potential of these enzymes for asym. synthesis is illustrated with recent examples, describing the prepn. of some biol. active mols.

L10 ANSWER 29 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
1999:4218 Document No. 130:181528 Effect of carbon and nitrogen sources on the production of a highly enantioselective ***epoxide*** ***hydrolase*** from ***Aspergillus*** niger. Morisseau, C.; Venturi, G.; Moussou, P.; Baratti, J. (Faculte des Sciences de Luminy, Biocatalysis and Fine Chemistry group, Marseille, 13288, Fr.). Biotechnology Techniques, 12(11), 805-809 (English) 1998. CODEN: BTECE6. ISSN: 0951-208X. Publisher: Chapman & Hall.
AB The highly enantioselective ***epoxide*** ***hydrolase*** (EH) from ***Aspergillus*** niger is well utilized as biocatalysts for the prepn. of enantiopure chiral epoxides and diols. Both growth of the fungus and EH activity prodn. were found greatly affected by changing the carbon or the nitrogen source with fructose and corn steep liquor being the best. Their concns. were optimized (10 g.l-1 of fructose and 15 g.l-1 of corn steep) which resulted in an increase of both the biomass produced (31%) and the ***epoxide*** ***hydrolase*** specific activity (38%). The results obtained suggested a complex regulation of the EH prodn. On the whole, a two times increase of the total EH activity was obtained.

L10 ANSWER 30 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
1998:804940 Document No. 130:150750 Microbiological transformations 41. Screening for novel fungal ***epoxide*** ***hydrolases*** . Moussou, Philippe; Archelas, Alain; Furstoss, Roland (Fac. Sci. Luminy, Univ. Mediterranee, Marseille, 901, Fr.). Journal of Molecular Catalysis B: Enzymatic, 5(5-6), 447-458 (English) 1998. CODEN: JMCEF8. ISSN: 1381-1177. Publisher: Elsevier Science B.V..
AB A search for new fungal ***epoxide*** ***hydrolases*** is described, which led to the selection of 7 strains of interest. The biol. hydrolysis of various alkyl and aryl epoxides using whole cells of these 7 strains is described. The enantio- and regio-selectivity obsd. proved to be variable depending upon the type of fungus and the substrate structure. However, a general trend was the preferential formation of the diol with (R) abs. configuration at the C atom beating the bulkier substituent.

L10 ANSWER 31 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
1998:533834 Document No. 129:259352 Fungal ***epoxide*** ***hydrolases*** : new tools for the synthesis of enantiopure epoxides and diols. Archelas, Alain (URA CNRS 1320, Groupe de Chimie Organique et Bioorganique, Faculte des Sciences de Luminy, Marseille, F-13288, Fr.). Journal of Molecular Catalysis B: Enzymatic, 5(1-4), 79-85 (English) 1998. CODEN: JMCEF8. ISSN: 1381-1177. OTHER SOURCES: CASREACT 129:259352. Publisher: Elsevier Science B.V..
AB This presentation describes efficient means of prepg. optically pure epoxides and diols using fungal ***epoxide*** ***hydrolases*** as biocatalysts. The biohydrolyzes can be carried out in a preparative scale for different types of epoxides as terpenic, aliph., arom., and glycidyl acetal derivs. bearing an epoxide moiety. In addn., in order to obtain these compds. in good yield, an efficient enzymic reactor and different enantioconvergent processes were devised.

L10 ANSWER 32 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
1998:454228 Document No. 129:175498 Microbiological transformations. part 42: a two-liquid-phase preparative scale process for an ***epoxide*** ***hydrolase*** catalyzed resolution of para-bromo-.alpha.-methyl styrene oxide. occurrence of a surprising enantioselectivity enhancement. Cleij, M.; Archelas, A.; Furstoss, R. (Groupe Biocatalyse et Chimie Fine, ERS 157 Associee au CNRS, Faculte des Sciences de Luminy, Marseille, 13288, Fr.). Tetrahedron: Asymmetry, 9(11), 1839-1842 (English) 1998. CODEN: TASYE3. ISSN: 0957-4166. OTHER SOURCES: CASREACT 129:175498.

Publisher: Elsevier Science Ltd..
AB A two liq.-phase process allowing for the preparative scale enantioselective resoln. of 80 g/L (i.e. 0.38 mol/L) para-bromo-.alpha.-Me styrene oxide is described, using an enzymic ext. from the fungus ***Aspergillus*** niger. The life time of the enzyme, and therefore the efficiency of the biohydrolysis, was considerably improved by performing this biohydrolysis at 4.degree.C. Surprisingly, the use of this procedure led to a dramatic enhancement of the reaction enantioselectivity.

L10 ANSWER 33 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
1998:223436 Document No. 128:294641 Kinetic resolution for optically active epoxides by microbial enantioselective hydrolysis. Choi, Won Jae; Huh, Eun Chul; Park, Hyoung Jun; Lee, Eun Yeol; Choi, Cha Yong (Department of Chemical Technology, College of Engineering, Seoul National University, Seoul, 151-742, S. Korea). Biotechnology Techniques, 12(3), 225-228 (English) 1998. CODEN: BTECE6. ISSN: 0951-208X. Publisher: Chapman & Hall.
AB Resoln. of several racemic epoxides was accomplished using the ***epoxide*** ***hydrolase*** activity of whole cells of the freshly isolated ***Aspergillus*** niger. (S)-Styrene oxide, for example, was obtained from its racemate with optical purity of 100% ee and 32% yield.

L10 ANSWER 34 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
1997:272044 Document No. 126:342505 Asymmetric hydrolysis of racemic para-nitrostyrene oxide using an ***epoxide*** ***hydrolase*** preparation from ***Aspergillus*** niger. Morisseau, Christophe; Nellaiah, Hariharan; Archelas, Alain; Furstoss, Roland; Baratti, Jacques C. (ERS CNRS 157, Biocatalysis and Fine Chemistry, Marseille, 13288, Fr.). Enzyme and Microbial Technology, 20(6), 446-452 (English) 1997. CODEN: EMTED2. ISSN: 0141-0229. Publisher: Elsevier.
AB A lyophilized ***epoxide*** ***hydrolase*** prepn. was isolated from the fungus ***Aspergillus*** niger. The prepn. could be used in place of the whole mycelium as biocatalyst for the enantioselective hydrolysis of racemic para-nitrostyrene oxide. The cosolvent used for substrate dissoln. showed slightly different effects on enzyme activity and stability. Dimethylsulfoxide (DMSO) was selected as the less inhibitory cosolvent among those tested. The enzyme prepn. was first proved efficient by running a batch reactor at a low substrate concn. of 4 mM. The hydrolysis of para-nitrostyrene oxide was fast (around 5 h) and with high enantioselectivity (E = 41). The (S) enantiomer of the epoxide remained in the reaction mixt. with an enantiomeric excess (ee) higher than 97% for a conversion of 47%. The substrate concn. had been optimized. It could be increased to 330 mM (54 g L-1) without affecting the ee; therefore, the method is potentially useful for the preparative resoln. of epoxides. Applications are in the field of chiral synthons which are important building blocks in org. synthesis.

L10 ANSWER 35 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
1996:590221 Document No. 125:216582 Microbiological transformations. 33. Fungal ***epoxide*** ***hydrolases*** applied to the synthesis of enantiopure para-substituted styrene oxides. A mechanistic approach. Pedragosa-Moreau, S.; Morisseau, C.; Zylber, J.; Archelas, A.; Baratti, J.; Furstoss, R. (Groupe Biocatalyse et Chimie Fine, Faculte des Sciences de Luminy, Marseille, 13288, Fr.). Journal of Organic Chemistry, 61(21), 7402-7407 (English) 1996. CODEN: JOCEAH. ISSN: 0022-3263. Publisher: American Chemical Society.
AB The biohydrolysis of differently para-substituted styrene oxide derivs. was studied, using whole cells of the fungi ***Aspergillus*** niger or Beauveria sulfurescens. These microorganisms proved to be equipped with ***epoxide*** ***hydrolases*** which are able to achieve these hydrolyses with high enantioselectivity. This allowed the prepn. of the optically active epoxides and of the corresponding vicinal diols which were obtained with good to excellent enantiomeric purity. These two microorganisms proved to be enantiocomplementary. A mechanistic study, carried out using a crude lyophilized enzymic ext. from A. niger, indicated via Hammet coeff. plotting that this hydrolysis is very probably due to a general base-catalyzed process.

L10 ANSWER 36 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
1996:380148 Document No. 125:56385 Biological resolution of racemic indene oxide to (1S,2R)-indene oxide. Chartrain, Michel M.; Senanayake, Chris

H.; Rosazza, John P. N.; Zhang, Jinyou (Merck and Co., Inc., USA). PCT Int. Appl. WO 9612818 A1 19960502, 44 pp. DESIGNATED STATES: W: CA, JP; RW: AT, BE, CH, DE, DK, ES, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1995-US13297 19951017. PRIORITY: US 1994-326985 19941021.

AB A process is disclosed that hydrolyzes, by the action of an ***epoxide*** ***hydrolase*** of Diplodia gossypina ATCC 16391 or ATCC 10936, the undesired enantiomer of racemic indene oxide, an epoxide of indane. The optically pure compd. produced is used as an intermediate in the synthesis of compds. that inhibit HIV protease and thus are useful in the prevention or treatment of infection by the human immunodeficiency virus (HIV).

L10 ANSWER 37 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN

1996:216556 Document No. 124:253992 Microbial ***epoxide*** ***hydrolases*** . Faber, Kurt; Mischitz, martin; Kroutil, Wolfgang (Inst. Org. Chem., Graz Univ. Technol., Graz, A-8010, Austria). Acta Chemica Scandinavica, 50(3), 249-58 (English) 1996. CODEN: ACHSE7. ISSN: 0904-213X. Publisher: Munksgaard.

AB A review with 66 refs. Chiral epoxides and 1,2-diols, which are central building blocks for the asym. synthesis of bioactive compds., can be obtained by using enzymes, which catalyze the enantioselective hydrolysis of epoxides - ***epoxide*** ***hydrolases*** . These biocatalysts are more widely distributed in fungi and bacteria than previously expected, and sufficient sources from bacteria, such as Rhodococcus and Myobacterium sp., or fungi, for instance ***Aspergillus*** and Beauveria sp. have recently been identified. The reaction proceeds via an SN2-specific opening of the epoxide leading to the formation of the corresponding trans-configurated 1,2-diols. For the resoln. of 2-monosubstituted epoxides and for 2,2-disubstituted substrates fungal cells and several bacteria, resp., have been shown to possess excellent selectivities. In addn., the use of non-natural nucleophiles such as azide or amine provides access to chiral azido- and amino-alcs. The synthetic potential of these enzymes is illustrated with recent examples of kinetic resolns. of epoxides from the literature.

L10 ANSWER 38 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN

1996:197532 Document No. 124:283953 Microbiological transformations. 32. Use of ***epoxide*** ***hydrolase*** mediated biohydrolysis as a way to enantiopure epoxides and vicinal diols: application to substituted styrene oxide derivatives. Pedragosa-Moreau, S.; Archelas, A.; Furstoss, R. (Groupe Chimie Organique Bioorganique, Faculte des Sciences de Luminy, Marseille, 13288, Fr.). Tetrahedron, 52(13), 4593-606 (English) 1996. CODEN: TETRAB. ISSN: 0040-4020. Publisher: Elsevier.

AB The biohydrolyses of various substituted styrene oxide derivs. using the fungi ***Aspergillus*** niger or Beauveria sulfurescens are described. The results obtained show that this methodol. allows the prepn. of enantiomerically enriched epoxides and diols via enantioselective and regioselective hydration. The comparative study of he results obtained suggests that these hydrolyses operate following different mechanisms and a model of he corresponding active sites is proposed.

L10 ANSWER 39 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN

1995:1002124 Document No. 124:53760 Enantioselective hydrolysis of p-nitrostyrene oxide by an ***epoxide*** ***hydrolase*** preparation from ***Aspergillus*** niger. Nellaiah, Hariharan; Morisseau, Christophe; Archelas, Alain; Furstoss, Roland; Baratti, Jacques C. (Groupe Chimie Organique Bioorganique, CNRS, Marseille, 13288, Fr.). Biotechnology and Bioengineering, 49(1), 70-7 (English) 1996. CODEN: BIBIAU. ISSN: 0006-3592. Publisher: Wiley.

AB The ***epoxide*** ***hydrolase*** activity of A. niger was synthesized during growth of the fungus and is assocd. with the sol. cell fraction. An enzyme prepn. was worked out which could be used in place of the whole mycelium as biocatalyst for the hydrolysis of epoxides. The effects of 4 different cosolvents on enzyme activity were investigated. DMSO was selected for epoxide solubilization. The effect of temp. on both reaction rate and enzyme stability was studied in the presence of DMSO (0.2 vol. ratio). A temp. of 25.degree. was selected for the reaction of bioconversion. With a substrate concn. of 4.5 mM, a batch reactor showed that the enzyme prepn. hydrolyzed p-nitrostyrene oxide with very high enantioselectivity. The (S)-enantiomer of the epoxide remained in the

reaction mixt. and showed an enantiomeric excess >99%. The substrate concn. could be increased to 20 mM without affecting the enantiomeric excess and degree of conversion. Therefore, the method is potentially useful for the preparative resoln. of epoxides. Application are in the field of chiral synthons which are important building blocks in org. synthesis.

L10 ANSWER 40 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
1994:696890 Document No. 121:296890 Microbiological transformations-XXIX. Enantioselective hydrolysis of epoxides using microorganisms: a mechanistic study. Pedragosa-Moreau, S.; Archelas, A.; Furstoss, R. (Groupe Chimie Organique Bioorganique, URA CNRS, Marseille, 13288, Fr.). Bioorganic & Medicinal Chemistry, 2(7), 609-16 (English) 1994. CODEN: BMECEP. ISSN: 0968-0896. Publisher: Elsevier.
AB The regio- and stereochem. of the hydrolysis of styrene oxide by two fungi: ***Aspergillus*** niger and Beauveria sulfurescens, were studied using H218O labeling expts. Also, the kinetic parameters of these hydrolyses were detd. We conclude that the ***epoxide*** ***hydrolases*** of these two fungi operate via different mechanisms.

L10 ANSWER 41 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
1988:544395 Document No. 109:144395 Effect of inducers on metabolism of benzo[a]pyrene in vivo and in vitro: analysis by high pressure liquid chromatography. Datta, Debjani; Samanta, Timir B. (Dep. Microbiol., Bose Inst., Calcutta, 700009, India). Biochemical and Biophysical Research Communications, 155(1), 493-502 (English) 1988. CODEN: BBRCA9. ISSN: 0006-291X.
AB The characterization of metabolites formed from benzo[a]pyrene (BP) by ***Aspergillus*** ochraceus TS and effect of inducers on BP metab. are reported. The HPLC profile of BP metabolites was similar to that of mammalian microsomes furnishing diols, quinones, and phenols. The prodn. of BP-4,5-dihydrodiol (K-region diol) by A. ochraceus TS seems to be novel and provides the 1st report on BP metab. by eukaryotic fungi. In control, phenols and quinones were produced in excess over dihydrodiols, whereas the induced prepn. showed the reverse order. Presumably the induction effecting prodn. of excess dihydrodiols influenced the synthesis of ***epoxide*** ***hydrolase*** . In addn., a differential increase in BP metab. was obsd. with inducers of narrow and broad specificity.

L10 ANSWER 42 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
1978:131677 Document No. 88:131677 Reactivity of 12,13-epoxytrichothecenes with ***epoxide*** ***hydrolase*** , glutathione-S-transferase and glutathione. Nakamura, Yasuko; Ohta, Minoru; Ueno, Yoshio (Fac. Pharm. Sci., Tokyo Univ. Sci., Tokyo, Japan). Chemical & Pharmaceutical Bulletin, 25(12), 3410-14 (English) 1977. CODEN: CPBTAL. ISSN: 0009-2363.
AB Interaction of the 12,13-epoxytrichothecenes and related mycotoxins with ***epoxide*** ***hydrolase*** [***9048-63-9***] and glutathione S-transferase (GSH-S-transferase) [50812-37-8] from rat liver was examd. in vitro. Neither hydrolysis of safrole oxide [7470-44-2] by the microsomal ***epoxide*** ***hydrolase*** nor conjugation of 2,3-epoxy-(p-nitrophenoxy)propane [5255-75-4] with glutathione [70-18-8] by the sol. GSH-S-transferase was interfered by the trichothecenes such as T-2 toxin [21259-20-1] and fusarenon-X [23255-69-8]. Gas-liq. chromatog. (GLC) anal. and colorimetric detn. of the residual GSH revealed that the trichothecenes were inert to the partially purified GSH-S-transferase. In contrast to the trichothecenes, PR-toxin [56299-00-4], an epoxide mycotoxin from Penicillium roqueforti, and lactones such as patulin [149-29-1] and penicillic acid [90-65-3] from Penicillium and ***Aspergillus*** spp., were found to react nonenzymically with GSH in a molar ratio of 1:1.

L10 ANSWER 43 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
1956:5183 Document No. 50:5183 Original Reference No. 50:1127b-f Production of trans-l-epoxysuccinic acid by fungi and its microbiological conversion to meso-tartaric acid. Martin, William R.; Foster, J. W. (Univ. of Texas, Austin). Journal of Bacteriology, 70, 405-14 (Unavailable) 1955. CODEN: JOBAAY. ISSN: 0021-9193.
AB A soil isolate of ***Aspergillus*** fumigatus produced appreciable quantities of trans-l-epoxy-succinic acid (EPO) from glucose or alc. as substrates. The acid was isolated in cryst. form and characterized by

several criteria. Several fungi, bacteria, and a yeast capable of using EPO salts as the sole source of C were isolated from soil. One bacterium, identified as a Flavobacterium sp. would oxidize EPO salts and the synthetic racemic trans-dl-epoxysuccinate, but not the geometric isomer, cis-epoxy-succinic acid. Cell-free enzymic exts. converted EPO salts to meso-tartrate. This is the first reported natural occurrence of meso-tartrate. The free acid was isolated in cryst. form, characterized chemically, and identified by the x-ray diffraction pattern of the Ca salt. The enzyme has been named trans-succinicepoxide hydrolase and apparently requires no dialyzable cofactor. Whole cells of Flavobacterium sp. harvested from EPO medium were simultaneously adapted to oxidize meso-tartrate but not d- or l-tartrates. Whole cells isolated from meso-tartrate medium did not oxidize d- or l-tartrate but did oxidize EPO salts only after a short lag period. Exts. of meso-tartrate cells contained no trans-succinicepoxide hydrolase activity; hence, these cells were not back adapted to EPO salts. These data seem to indicate that the first stage in the utilization of epoxysuccinate by these bacteria is via meso-tartrate. Proof that meso-tartrate is formed from EPO salts by whole cells was obtained by the addn. of Ca++ to the medium. The intermediate meso-tartrate was trapped as the insol. Ca salt which crystd. in the medium. All the fungi, bacteria, and the yeast formed Ca meso-tartrate in this way. 23 references.

=> D 14-35 CBIB ABS

L11 ANSWER 14 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN
1999:369319 Document No. 131:141833 Multiple ***epoxide***
hydrolases in Alternaria alternata f. sp. lycopersici and their relationship to medium composition and host-specific toxin production. Morisseau, Christophe; Ward, Barney L.; Gilchrist, David G.; Hammock, Bruce D. (Department of Entomology, University of California, Davis, CA, 95616, USA). Applied and Environmental Microbiology, 65(6), 2388-2395 (English) 1999. CODEN: AEMIDF. ISSN: 0099-2240. Publisher: American Society for Microbiology.

AB The prodn. of Alternaria alternata f. sp. lycopersici host-specific toxins (AAL toxins) and ***epoxide*** ***hydrolase*** (EH) activity were studied during the growth of this plant-pathogenic ***fungus*** in stationary liq. cultures. Media contg. pectin as the primary carbon source displayed peaks of EH activity at day 4 and at day 12. When pectin was replaced by glucose, there was a single peak of EH activity at day 6. Partial characterization of the EH activities suggests the presence of three biochem. distinguishable EH activities. Two of them have a mol. mass of 25 kDa and a pI of 4.9, while the other has a mol. mass of 20 kDa and a pI of 4.7. Each of the EH activities can be distinguished by substrate preference and sensitivity to inhibitors. The EH activities present at day 6 (glucose) or day 12 (pectin) are concomitant with AAL toxin prodn.

L11 ANSWER 15 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN
1999:279765 Document No. 130:293281 Cloning and gene sequence encoding ***epoxide*** ***hydrolase*** from Rhodococcus rhodochrous. Dauvrin, Thierry; Deslee, Pascale (Puratos N.V., Belg.). Eur. Pat. Appl. EP 911392 A1 19990428, 21 pp. DESIGNATED STATES: R: AT, BE, CH, DE, DK, ES, FR, GB, GR, IT, LI, LU, NL, SE, MC, PT, IE, SI, LT, LV, FI, RO. (English). CODEN: EPXXDW. APPLICATION: EP 1997-870168 19971024.

AB The present invention is related to an isolated and purified nucleotidic sequence from microbial origin, encoding an ***epoxide*** ***hydrolase*** . The gene encoding ***epoxide*** ***hydrolase*** was isolated from Rhodococcus rhodochrous LMGP-18079, and encodes a protein 253 amino acids in length. The invention includes a vector comprising said nucleotidic sequence, the recombinant host cell transformed by said nucleotidic sequence, and the ***epoxide*** ***hydrolase*** amino acid sequence encoded by said nucleotidic sequence and/or expressed by said recombinant host cell. The ***epoxide*** ***hydrolase*** may be used for the hydrolysis of epoxides such as cis-epoxysuccinate, allowing retention of the L-+-form of tartaric acid which is used by the food industry.

L11 ANSWER 16 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN
1999:172639 Document No. 130:205916 Screening nucleic acid populations for

novel bioactivities. Short, Jay M. (Diversa Corporation, USA). PCT Int. Appl. WO 9910539 A1 19990304, 99 pp. DESIGNATED STATES: W: AU, CA, JP; RW: AT, BE, CH, CY, DE, DK, ES, FI, FR, GB, GR, IE, IT, LU, MC, NL, PT, SE. (English). CODEN: PIXXD2. APPLICATION: WO 1998-US17779 19980826. PRIORITY: US 1997-918406 19970826.

AB Disclosed is a process for identifying clones having a specified activity of interest, which process comprises (i) generating one or more expression libraries derived from nucleic acid directly isolated from the environment; and (ii) screening said libraries utilizing an assay system. More particularly, this is a process for identifying clones having a specified activity of interest by (i) generating one or more expression libraries derived from nucleic acid directly or indirectly isolated from the environment; (ii) exposing said libraries to a particular substrate or substrates of interest; and (iii) screening said exposed libraries utilizing a fluorescence activated cell sorter to identify clones which react with the substrate or substrates. Also provided is a process for identifying clones having a specified activity of interest by (i) generating one or more expression libraries derived from nucleic acid directly or indirectly isolated from the environment; (ii) screening said exposed libraries utilizing an assay requiring a binding event or the covalent modification of a target, and a fluorescence activated cell sorter to identify pos. clones.

L11 ANSWER 17 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN

1999:77985 Document No. 130:293060 ***Epoxide*** ***hydrolases*** from yeasts and other sources: versatile tools in biocatalysis. Weijers, Carel A. G. M.; de Bont, Jan A. M. (Department of Food Technology and Nutritional Sciences, Division of Industrial Microbiology, Wageningen Agricultural University, Wageningen, 6700 EV, Neth.). Journal of Molecular Catalysis B: Enzymatic, 6(3), 199-214 (English) 1999. CODEN: JMCEF8. ISSN: 1381-1177. Publisher: Elsevier Science B.V..

AB A review with 73 refs. Major characteristics, substrate specificities and enantioselectivities of ***epoxide*** ***hydrolases*** from various sources are described. ***Epoxide*** ***hydrolase*** activity in yeasts is discussed in more detail and is compared with activities in other microorganisms. Constitutively produced bacterial ***epoxide*** ***hydrolases*** are highly enantioselective in the hydrolysis of 2,2- and 2,3-disubstituted epoxides. A novel bacterial limonene-1,2- ***epoxide*** ***hydrolase*** , induced by growth on monoterpenes, showed high activities and selectivities in the hydrolysis of several substituted alicyclic epoxides. Constitutively produced ***epoxide*** ***hydrolases*** are found in eukaryotic microorganisms. Enzymes from filamentous ***fungi*** are useful biocatalysts in the resoln. of aryl- and substituted alicyclic epoxides. Yeast ***epoxide*** ***hydrolase*** activity has been demonstrated for the enantioselective hydrolysis of various aryl-, alicyclic- and aliph. epoxides by a strain of Rhodotorula glutinis. The yeast enzyme, moreover, is capable of asym. hydrolysis of meso epoxides and performs highly enantioselective resoln. of unbranched aliph. 1,2-epoxides. Screening for other yeast ***epoxide*** ***hydrolases*** shows that high enantioselectivity is restricted to a few basidiomycetes genera only. Resoln. of very high substrate concns. is possible by using selected basidiomycetes yeast strains.

L11 ANSWER 18 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN

1998:326808 Document No. 128:312353 Biodegradation and occurrence of four polycyclic aromatic hydrocarbons in aquatic sediments. Klimaszewska, Katarzyna (Inst. Systemow Inzynierii Srodowiska, Politechnika Warszawska, Warsaw, Pol.). Biotechnologia (1), 140-148 (Polish) 1998. CODEN: BIECEV. ISSN: 0860-7796. Publisher: Instytut Chemii Bioorganicznej PAN.

AB This review with 28 refs. outlines microbial degrdn. conditions of polycyclic arom. hydrocarbons in aquatic sediments. Microorganisms able to decomp. these compds. are discussed. Concns. of four polycyclic arom. hydrocarbons in various sediments are presented. Bacteria and ***fungi*** decomp. PAH's in different ways. Eucariota use monooxygenase, cytochrome P 450 and ***epoxide*** ***hydrolase*** to produce trans-dihydrodiols. Biodegrdn. of PAH's by procariota is due to dioxygnase activity. Bacteria transform these compds. to cis-dihydrodiols and then to more polar compds. with fewer arom. rings in the mol.

L11 ANSWER 19 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN
1998:282825 Document No. 129:24896 Microbiological Transformations. 38. Clues to the Involvement of a·General Acid Activation during Hydrolysis of Para-Substituted Styrene Oxides by a Soluble ***Epoxide*** ***Hydrolase*** from Syncephalastrum racemosum. Moussou, P.; Archelas, A.; Baratti, J.; Furstoss, R. (Groupe Biocatalyze et Chimie Fine ERS 157 associee au CNRS, Faculte des Sciences de Luminy Case 901, Marseille, 13288, Fr.). Journal of Organic Chemistry, 63(11), 3532-3537 (English) 1998. CODEN: JOCEAH. ISSN: 0022-3263. Publisher: American Chemical Society.

AB In the course of this work, we have detd. the regioselectivity as well as the rate of bio-hydrolysis of various para-substituted styrene oxide derivs. catalyzed by a new ***epoxide*** ***hydrolase*** activity found in the sol. cell ext. of the ***fungus*** Syncephalastrum racemosum. We have obsd. that this regioselectivity switched progressively from the benzylic C.alpha. carbon atom to the terminal C.beta. carbon atom depending upon the electronic character of the para substituent. Hammett plotting of the ratio of water incorporation at both the benzylic and terminal carbon atoms, i.e., log .alpha./.beta. vs. .sigma., gave linear relationships for the two (R)- and (S)-epoxide enantiomers with slopes .rho..alpha./.beta. = -2.07 and -1.35, resp. Apparent kinetic consts. Km and Vmax were detd. for the bio-hydrolysis of the enantiomers of R abs. configuration, which were the better substrates. Hammett correlation was investigated for Vmax/Km for the reaction on both the C.alpha. and C.beta. carbon atoms. Log .alpha.Vmax/Km vs. .sigma. gave a linear relationship with a slope .rho..alpha.Vmax/Km = -1.8, suggesting that, in the case of these enzyme/substrate couples, the rate-detg. step is the oxirane ring cleavage. These results give, for the first time, interesting clues to the fact that a general acid activation of the epoxide is very probably involved in a concerted process together with its nucleophilic attack.

L11 ANSWER 20 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN
1998:268826 Document No. 129:51914 Characterization of ***epoxide*** ***hydrolase*** activity in Alternaria alternata f. sp. lycopersici. Possible involvement in toxin production. ***Epoxide*** ***hydrolase*** in Alternaria alternata f. sp. lycopersici. Pinot, Franck; Caldas, Eloisa D.; Schmidt, Christina; Gilchrist, David G.; Jones, A. D.; Winter, Carl K.; Hammock, Bruce D. (Lab. Enzymologie Cellullaire Moleculaire, Inst. Biologie Moleculaire Plantes, Strasbourg, Fr.). Mycopathologia, 140(1), 51-58 (English) 1997. CODEN: MYCPAH. ISSN: 0301-486X. Publisher: Kluwer Academic Publishers.

AB The role of ***epoxide*** ***hydrolase*** (EH) was studied in the toxin producing ***fungus*** A. alternata f.sp. lycopersici (Aal). Its activity was detd. with the substrate trans-diphenylpropane oxide in subcellular fractions showing a predominant location in the 100,000.times.g supernatant with a pH optimum of 7.4. Increased toxin prodn. between days 3 and 9 over a 15 days period was concomitant with high EH activity while the activity remained const. in cultured A. alternata producing no toxin. In vivo treatment with the peroxisome proliferator clofibrate stimulated EH activity by 83% and enhanced toxin prodn. 6.3 fold. 4-Fluorochalcone oxide and (2S,3S)-(-)-3-(4-nitrophenyl)-glycidol inhibited EH activity in vitro with an I50 of 23 and 72 .mu.M, resp. The possible physiol. substrate 9,10-epoxystearic acid was hydrolyzed more efficiently than the model substrates trans- and cis-stilbene oxide and trans- and cis-diphenylpropane oxide.

L11 ANSWER 21 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN
1998:103996 Document No. 128:192498 Microbiological transformations. 40. Use of ***fungal*** ***epoxide*** ***hydrolases*** for the synthesis of enantiopure alkyl epoxides. Moussou, Philippe; Archelas, Alain; Furstoss, Roland (Groupe Biocatalyse et Chimie Fine, ERS 157 associee au CNRS, Faculte des Sciences de Luminy, Universite de la Mediterranee, Marseille, 13288, Fr.). Tetrahedron, 54(8), 1563-1572 (English) 1998. CODEN: TETRAB. ISSN: 0040-4020. Publisher: Elsevier Science Ltd..

AB The enantioselective biohydrolysis of various substituted alkyl-epoxides using seven different ***fungi*** are described. These strains were used to achieve the prepn. of these alkyl epoxides in high enantiomeric purity. A combined chemoenzymic process is also described, allowing to enhance the overall yield of such an approach.

L11 ANSWER 22 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN
1997:433783 Document No. 127:173603 Enzymic mechanisms involved in phenanthrene degradation by the white rot ***fungus*** Pleurotus ostreatus. Bezalel, Lea; Hadar, Yitzhak; Cerniglia, Carl E. (Dep. of Plant Pathol. and Microbiol., Fac. of Agric., Hebrew Univ. of Jerusalem, Rehovot, 76100, Israel). Applied and Environmental Microbiology, 63(7), 2495-2501 (English) 1997. CODEN: AEMIDF. ISSN: 0099-2240. Publisher: American Society for Microbiology.

AB The enzymic mechanisms involved in the degrdn. of phenanthrene by the white rot ***fungus*** Pleurotus ostreatus were examd. Phase I metab. (cytochrome P 450 monooxygenase and ***epoxide*** ***hydrolase***) and phase II conjugation (glutathione S-transferase, aryl sulfotransferase, UDP-glucuronosyltransferase, and UDP-glucosyltransferase) enzyme activities were detd. for mycelial exts. of P. ostreatus. Cytochrome P 450 was detected in both cytosolic and microsomal fractions at 0.16 and 0.38 nmol min-1 mg of protein1, resp. Both fractions oxidized [9,10-14C]phenanthrene to phenanthrene trans-9,10-dihydrodiol. The cytochrome P 450 inhibitors 1-aminobenzotriazole (0.1 mM), SKF-525A (proadifen, 0.1 mM), and carbon monoxide inhibited the cytosolic and microsomal P-450s differently. Cytosolic and microsomal ***epoxide*** ***hydrolase*** activities, with phenanthrene 9,10-oxide as the substrate, were similar, with specific activities of 0.50 and 0.41 nmol min-1 mg of protein-1, resp. The ***epoxide*** ***hydrolase*** inhibitor cyclohexene oxide (5 mM) significantly inhibited the formation of phenanthrene trans-9,10-dihydrodiol in both fractions. The phase II enzyme 1-chloro-2,4-dinitrobenzene glutathione S-transferase was detected in the cytosolic fraction (4.16 nmol min-1 mg of protein-1), whereas aryl adenosine-3'-phosphate-5'-phosphosulfate sulfotransferase (aryl PAPS sulfotransferase) UDP-glucuronosyltransferase, and UDP-glucosyltransferase had microsomal activities of 2.14, 4.25, and 4.21 nmol min-1 mg of protein-1, resp., with low activity in the cytosolic fraction. However, when P. ostreatus culture broth incubated with phenanthrene was screened for phase II metabolites, no sulfate, glutathione, glucoside, or glucuronide conjugates of phenanthrene metabolites were detected. These expts. indicate the involvement of cytochrome P 450 monooxygenase and ***epoxide*** ***hydrolase*** in the initial phase I oxidn. of phenanthrene to form phenanthrene trans-9,10-dihydrodiol. Laccase and manganese-independent peroxidase were not involved in the initial oxidn. of phenanthrene. Although P. ostreatus had phase II xenobiotic metabolizing enzymes, conjugation reactions were not important for the elimination of hydroxylated phenanthrene.

L11 ANSWER 23 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN
1997:373926 Document No. 127:146923 Biohydrolysis of substituted styrene oxides by Beauveria densa CMC 3240. Grogan, Gideon; Rippe, Catherine; Willetts, Andrew (Dep. Biol. Sci., Univ. Exeter, Exeter, EX4 4QG, UK). Journal of Molecular Catalysis B: Enzymatic, 3(5), 253-257 (English) 1997. CODEN: JMCEF8. ISSN: 1381-1177. Publisher: Elsevier.

AB Resting whole cell suspensions of the ***fungus*** B. densa CMC 3240 contg. an ***epoxide*** ***hydrolase*** were used to resolve a series of para-substituted styrene oxides, with stereoinversion of the hydrolyzed epoxide enantiomer. The regio- and hence, enantioselectivity of hydrolysis is compromised where ortho- and para-methyl- and chlorostyrene oxides are substrates. Negligible activity was obsd. with para-nitrostyrene oxide as substrate. The results appear to confirm a general mechanism of enzyme-catalyzed acid hydrolysis for Beauveria spp. acting on styrene oxides.

L11 ANSWER 24 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN
1996:445570 Document No. 125:136036 Novel aliphatic ***epoxide*** ***hydrolase*** activities from dematiaceous ***fungi*** . Grogan, Gideon; Roberts, Stanley M.; Willetts, Andrew J. (Department of Biological Sciences, Washington Singer Laboratories, University of Exeter, Exeter Devon, EX4 4QG, UK). FEMS Microbiology Letters, 141(2-3), 239-243 (English) 1996. CODEN: FMLED7. ISSN: 0378-1097. Publisher: Elsevier.

AB ***Epoxide*** ***hydrolases*** were found to be constitutively expressed in dematiaceous ***fungi*** coincident with secondary metabolite pigment prodn. in stationary or idiophase. Washed-cell prepns. of two ***fungi*** , Ulocladium atrum CMC 3280 and Zopfiella

karachiensis CMC 3284, exhibited affinity for 2,2-dialkylated oxiranes, for which contrasting enantioselectivities were obsd., but not for arom. styrene oxide or alicyclic cyclohexene oxide type substrates. Lyophilized prepns. of sol. ***epoxide*** ***hydrolase*** activities proved to be effective catalysts for the mild hydrolysis of aliph. epoxides.

L11 ANSWER 25 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN
1996:395524 Document No. 125:53292 Metabolism of phenanthrene by the white root ***fungus*** Pleurotus ostreatus. Zezalei, Lea; Hadar, Yitzhak; Fu, Peter P.; Freeman, James P.; Cerniglia, Carl E. (Dep. Plant Pathol. Microbiol., Hebrew Univ. jerusalem, Rehovot, 76100, India). Applied and Environmental Microbiology, 62(7), 2547-2553 (English) 1996. CODEN: AEMIDF. ISSN: 0099-2240. Publisher: American Society for Microbiology.
GI

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AB The white rot ***fungus*** Pleurotus ostreatus, grown for 11 days in basidiomycetes rich medium contg. [14C]phenanthrene, metabolized 94% of the phenanthrene (I) added. Of the total radioactivity, 3% was oxidized to CO2. Approx. 52% of I was metabolized to phenanthrene trans-9,10-dihydrodiol (II) (28%), 2,2'-diphenic acid (III) (17%), and unidentified metabolites (7%). Nonextractable metabolites accounted for 35% of the total radioactivity. The metabolites were extd. with ethylacetate, sepd. by reversed-phase high-performance liq. chromatog., and characterized by 1H NMR, mass spectrometry, and UV spectroscopy analyses. 18O2-labeling expts. indicated that one atom of oxygen was incorporated into the II. CD spectra of the II indicated that the abs. configuration of the predominant enantiomer was 9R,10R, which is different from that of the principal enantiomer produced by Phanerochaete chrysosporium. Significantly less II was obsd. in incubations with the cytochrome P 450 inhibitor SKF 525-A (77% decrease), 1-aminobenzotriazole (83% decrease), or fluoxetine (63% decrease). These expts. with cytochrome P 450 inhibitors and 18O2 labeling and the formation of II as the predominant metabolite suggest that P. ostreatus initially oxidizes I stereoselectively by a cytochrome P 450 monoxygenase and that this is followed by ***epoxide*** ***hydrolase*** -catalyzed hydration reactions.

L11 ANSWER 26 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN
1996:295502 Document No. 125:58219 Microbiological transformations. 31: Synthesis of enantiopure epoxides and vicinal diols using ***fungal*** ***epoxide*** ***hydrolase*** mediated hydrolysis. Pedragosa-Moreau, S.; Archelas, A.; Furstoss, R. (Groupe "Biocatalyse Chim. Fine", Fac. Sci. Luminy, Marseille, F-13288, Fr.). Tetrahedron Letters, 37(19), 3319-3322 (English) 1996. CODEN: TELEAY. ISSN: 0040-4039. Publisher: Elsevier.
AB The enantioselective hydrolysis of epoxyindene and dihydronaphthalene epoxides by the ***fungus*** Beauveria sulfurescens (ATCC 7159) is described. The reactants were (.+-.)-1a,6a-dihydro-6H-indeno[1,2-b]oxirene, (.+-.)-1a,2,3,7b-tetrahydronaphth[1,2-b]oxirene and (.+-.)-phenyloxirane. This allowed the prepn. of both these epoxides, as well as of the corresponding diols, in good to excellent enantiomeric purity.

L11 ANSWER 27 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN
1995:855385 Document No. 124:86723 Chiral bio-resolution of racemic indene oxide by ***fungal*** ***epoxide*** ***hydrolases*** . Zhang, Jinyou; Reddy, Jay; Roberge, Christopher; Senanayake, Chris; Greasham, Randolph; Chartrain, Michel (Merck Research Laboratories, Rahway, NJ, 07065, USA). Journal of Fermentation and Bioengineering, 80(3), 244-6 (English) 1995. CODEN: JFBIEX. ISSN: 0922-338X. Publisher: Society for Fermentation and Bioengineering, Japan.
AB Eighty ***fungal*** strains were evaluated for their prodn. of an ***epoxide*** ***hydrolase*** capable of catalyzing the kinetic resoln. of racemic indene oxide into 1(S),2(R)-indene oxide. This screen identified Diplodia gossipina ATCC 163991 as the best catalyst. Process development studies of this bio-resoln. demonstrated that the optical purity of the 1(S),2(R)-indene oxide produced was dependent upon pH and

substrate concn. A shake-flask-scale bio-resoln. process supported the prodn. of preparative quantities of optically pure (ee=100%) 1(S),2(R)-indene oxide.

L11 ANSWER 28 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN
1995:663893 Document No. 123:81633 Asymmetric microbial hydrolysis of epoxides. Mischitz, M.; Kroutil, W.; Wandel, U.; Faber, K. (Inst. Org. Chem., Graz Univ. Technology, Graz, A-8010, Austria). Tetrahedron: Asymmetry, 6(6), 1261-72 (English) 1995. CODEN: TASYE3. ISSN: 0957-4166. Publisher: Elsevier.
AB Kinetic resoln. of 2-mono- and 2,2-disubstituted epoxides was accomplished using ***epoxide*** ***hydrolases*** from bacterial and ***fungal*** origin by employing lyophilized whole microbial cells. In all cases investigated, the biocatalytic hydrolysis proceeded with retention of configuration at the stereogenic center leading to 1,2-diols and remaining epoxides. The selectivity of the reaction was dependent on the substrate structure and the strain used, with E-values ranging from low or moderate (with 2-monosubstituted epoxides) to excellent (E >100 with 2,2-disubstituted oxiranes).

L11 ANSWER 29 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN
1993:645059 Document No. 119:245059 Enantiomeric composition of the trans-dihydrodiols produced from phenanthrene by ***fungi*** . Sutherland, John B.; Fu, Peter P.; Yang, Shen K.; Von Tungeln, Linda S.; Casillas, Robert P.; Crow, Sidney A.; Cerniglia, Carl E. (Natl. Cent. Toxicol. Res., Food Drug Adm., Jefferson, AR, 72079, USA). Applied and Environmental Microbiology, 59(7), 2145-9 (English) 1993. CODEN: AEMIDF. ISSN: 0099-2240.
AB The trans-dihydrodiols produced during the metab. of phenanthrene by Cunninghamella elegans, Syncephalastrum racemosum, and Phanerochaete chrysosporium were purified by HPLC. The enantiomeric compns. and optical purities of the trans-dihydrodiols were detd. to compare interspecific differences in the regio- and stereoselectivity of the ***fungal*** enzymes. CD spectra of the trans-dihydrodiols were obtained, and the enantiomeric compn. of each prepn. was analyzed by HPLC with a chiral stationary-phase column. The phenanthrene trans-1,2-dihydrodiol produced by C. elegans was a mixt. of the 1R,2R and 1S,2S enantiomers in variable proportions. The phenanthrene trans-3,4-dihydrodiol produced by P. chrysosporium was the optically pure 3R,4R enantiomer, but that produced by S. racemosum was a 68:32 mixt. of the 3R,4R and 3S,4S enantiomers. The phenanthrene trans-9,10-dihydrodiol produced by P. chrysosporium was predominantly the 9S,10S enantiomer, but those produced by C. elegans and S. racemosum were predominantly the 9R,10R enantiomers. Thus, although different ***fungi*** may exhibit similar regioselectivity, there still may be differences in stereoselectivity that depend on the species and the cultural conditions.

L11 ANSWER 30 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN
1992:18202 Document No. 116:18202 Metabolism of phenanthrene by Phanerochaete chrysosporium. Sutherland, John B.; Selby, Allison L.; Freeman, James P.; Evans, Frederick E.; Cerniglia, Carl E. (Natl. Cent. Toxicol. Res., Food Drug Adm., Jefferson, AR, 72079, USA). Applied and Environmental Microbiology, 57(11), 3310-16 (English) 1991. CODEN: AEMIDF. ISSN: 0099-2240.
AB The white rot ***fungus*** P. chrysosporium metabolized phenanthrene when it was grown for 7 days at 37.degree. in a medium contg. malt ext., D-glucose, D-maltose, yeast ext., and Tween 80. After cultures were grown with [9-14C]phenanthrene, radioactive metabolites were extd. from the medium with EtOAcetate, sepd. by HPLC, and detected by liq. scintillation counting. Metabolites from cultures grown with unlabeled phenanthrene were identified as phenanthrene trans-9,10-dihydrodiol, phenanthrene trans-3,4-dihydrodiol, 9-phenanthrol, 3-phenanthrol, 4-phenanthrol, and the novel conjugate 9-phenanthryl .beta.-D-glucopyranoside. Identification of the compds. was based on their UV absorption, mass, and NMR spectra. Since lignin peroxidase was not detected in the culture medium, these results suggest the involvement of monooxygenase and ***epoxide*** ***hydrolase*** activity in the initial oxidn. and hydration of phenanthrene by P. chrysosporium.

L11 ANSWER 31 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN
1988:220464 Document No. 108:220464 The role of rat liver microsomal enzymes

in the metabolism of the ***fungal*** metabolite fusarin C. Gelderblom, W. C. A.; Thiel, P. G.; Van der Merwe, K. J. (Res. Inst. Nutr. Dis., South African Med. Res. Counc., Tygerberg, 7505, S. Afr.). Food and Chemical Toxicology, 26(1), 31-6 (English) 1988. CODEN: FCTOD7. ISSN: 0278-6915.

GI

/ Structure 2 in file .gra /

AB The metabolic activation of fusarin C (I; R1 = Me) by a rat liver microsomal monooxygenase resulted in the formation of a water-sol. mutagenic metabolite. However, fusarin C incubated in the presence of a microsomal prepn., but in the absence of an NADPH-generating system, led to the formation of fusarin PM1 (II; R1 = H), a highly water-sol. compd. which, like fusarin C, requires metabolic activation to be mutagenic. Enzyme studies using as substrates fusarins A and D, compds. structurally related to I, together with structural studies of II indicated that II was formed by the action of carboxylesterase which hydrolyses the C-20 Me ester group to a free carboxylic acid.

L11 ANSWER 32 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN

1984:587677 Document No. 101:187677 Effects of a fluoro substituent on the ***fungal*** metabolism of 1-fluoronaphthalene. Cerniglia, Carl E.; Miller, Dwight W.; Yang, Shen K.; Freeman, J. P. (Natl. Cent. Toxicol. Res., Food Drug Adm., Jefferson, AR, 72079, USA). Applied and Environmental Microbiology, 48(2), 294-300 (English) 1984. CODEN: AEMIDF. ISSN: 0099-2240.

GI

/ Structure 3 in file .gra /

AB The metab. of 1-fluoronaphthalene (I) by Cunninghamella elegans ATCC 36112 was studied. The metabolites were isolated by reverse-phase high-pressure liq. chromatog. and characterized by the application of UV absorption, 1H NMR, and mass spectral techniques. C. elegans Oxidized 1-fluoronaphthalene predominantly at the 3,4- and 5,6-positions to form trans-3,4-dihydroxy-3,4-dihydro-1-fluoronaphthalene and trans-5,6-dihydroxy-5,6-dihydro-1-fluoronaphthalene. In addn., 1-fluoro-8-hydroxy-5-tetralone, 5-hydroxy-1-fluoronaphthalene, and 4-hydroxy-1-fluoronaphthalene as well as glucoside, sulfate, and glucuronic acid conjugates of these phenols were formed. CD spectra of the trans-3,4- and trans-5,6-dihydrodiols formed from 1-fluoronaphthalene indicated that the major enantiomers of the dihydrodiols have S,S abs. stereochemistries. In contrast, the trans-5,6-dihydrodiol formed from 1-fluoronaphthalene from 3-methylcholanthrene-treated rats had Cotton effects that are opposite in sign (R,R) to those formed by C. elegans. The results indicate that the ***fungal*** monooxygenase-***epoxide*** ***hydrolase*** systems are highly stereoselective in the metab. of 1-fluoronaphthalene and that a fluoro substituent blocks epoxidn. at the fluoro-substituted double bond, decreases oxidn. at the arom. double bond that is peri to the fluoro substituent, and enhances metab. at the 3,4- and 5,6-positions of 1-fluoronaphthalene.

L11 ANSWER 33 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN

1984:19054 Document No. 100:19054 Regio- and stereoselective metabolism of 4-methylbenz[a]anthracene by the ***fungus*** Cunninghamella elegans. Cerniglia, Carl E.; Fu, Peter P.; Yang, Shen K. (Natl. Cent. Toxicol. Res., Food Drug Adm., Jefferson, AR, 72079, USA). Biochemical Journal, 216(2), 377-84 (English) 1983. CODEN: BIJOAK. ISSN: 0306-3275.

AB C. elegans Metabolized 4-methylbenz[a]anthracene [316-49-4] primarily at the Me group, this being followed by further metab. at the 8,9- and 10,11-positions to form trans-8,9-dihydro-8,9-dihydroxy-4-hydroxymethylbenz[a]anthracene and trans-10,11-dihydro-10,11-dihydroxy-4-hydroxymethylbenz[a]anthracene. There was no detectable trans-dihydrodiol formed at the Me-substituted double bond (3,4-positions) or at the K region (5,6-positions). The metabolites were isolated by reversed-phase high-pressure liq. chromatog. and characterized by the application of

UV-visible-absorption-, 1H NMR and mass-spectral techniques. The 4-hydroxymethylbenz[a]anthracene trans-8,9- and -10,11-dihydrodiols were optically active. Comparison of the CD spectra of the trans-dihydrodiols formed from 4-methylbenz[a]anthracene by C. elegans with those of the corresponding benz[a]anthracene trans-dihydrodiols formed by rat liver microsomal fraction indicated that the major enantiomers of the 4-hydroxymethylbenz[a]anthracene trans-8,9-dihydrodiol and trans-10,11-dihydrodiol formed by C. elegans have S.S abs. stereochemistries., which are opposite to those of the predominantly 8R,9R- and 10R,11R-dihydrodiols formed by the microsomal fraction. Incubation of C. elegans with 4-methylbenz[a]anthracene under 18O and subsequent mass-spectral anal. of the metabolites indicated that hydroxylation of the Me group and the formation of trans-dihydrodiols are catalyzed by cytochrome P 450 [9035-51-2] monooxygenase and ***epoxide*** ***hydrolase*** [***9048-63-9***] enzyme systems. Apparently, the ***fungal*** monooxygenase- ***epoxide*** ***hydrolase*** enzyme systems are highly stereo- and regio-selective in the metab. of 4-methylbenz[a]anthracene.

L11 ANSWER 34 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN

1982:541438 Document No. 97:141438 Metabolism of xenobiotic compounds by enzymes in cell extracts of the ***fungus*** Cunninghamella elegans. Wackett, Lawrence P.; Gibson, David T. (Dep. Microbiol., Univ. Texas, Austin, TX, 78712, USA). Biochemical Journal, 205(1), 117-22 (English) 1982. CODEN: BIJOAK. ISSN: 0306-3275.

AB Cell exts. of the filamentous ***fungus*** C. elegans contained ***epoxide*** ***hydrolase*** (EC 3.3.2.3), glutathione S-transferase (EC 2.5.1.18), and UDP-glucuronosyltransferase (EC 2.4.1.17) activities. ***Epoxide*** ***hydrolase*** activity was detd. with p-nitrostyrene oxide as substrate and was shown to be assocd. with the 100,000-g pellet obtained from disrupted mycelia. Glutathione S-transferase activity was demonstrated with 1-chloro-2,4-dinitrobenzene and p-nitrobenzyl chloride as substrates. The presence of 2 or more glutathione S-transferase activities was indicated by different activity ratios for the 2 substrates in different exts., and by distinct thermal denaturation curves. UDP-glucuronosyltransferase activity with 3-hydroxybenzo[a]pyrene as substrate was found only with the nonsedimentable fraction prepd. from ruptured mycelia.

L11 ANSWER 35 OF 35 CAPLUS COPYRIGHT 2004 ACS on STN

1975:94646 Document No. 82:94646 Fate of naturally occurring epoxy acid. Soluble epoxide hydrase, which catalyzes cis hydration, from Fusarium solani pisi. Kolattukudy, P. E.; Brown, Linda (Dep. Agric. Chem., Washington State Univ., Pullman, WA, USA). Archives of Biochemistry and Biophysics, 166(2), 599-607 (English) 1975. CODEN: ABBIA4. ISSN: 0003-9861.

AB A cell-free ext. prepd. from F. solani pisi grown on cutin, catalyzed the hydration of 18-hydroxy-9,10-epoxyoctadecanoic acid to 9,10,18-trihydroxyoctadecanoic acid while exts. from glucose-grown cells contained <6% of this activity. The product was identified by chromatog. techniques and by radio gas-liq. chromatog. of its periodate oxidn. products. This epoxide hydrase activity had a pH optimum at 9.0 and it was located mainly in the 100,000g supernatant fraction. Rate of hydration of the epoxy acid was linear up to 15 min and up to a protein concn. of 30 .mu.g/ml. This ***fungal*** epoxide hydrase has a mol. wt. of 35,000, as detd. by Sephadex G-100 gel filtration. It was partially purified by ammonium sulfate fractionation and gel filtration. The apparent Km and V of the enzyme was 2 .times. 10-4M and 222 nmoles/min/mg, resp. Parachloromercuribenzoate strongly inhibited the enzyme, while N-ethylmaleimide was a less potent inhibitor. 1,1,1-Trichloropropylene-2,3-oxide at 10-3M gave 50% inhibition of the hydration of 18-hydroxy-9,10-epoxyoctadecanoic acid. Kinetic anal. showed that trichloropropylene oxide was a competitive inhibitor. 18-Acetoxy-9,10-epoxyoctadecanoic acid, Me 18-acetoxy-9,10-epoxyoctadecanoate, 9,10-epoxyoctadecanoic acid, and styrene oxide were not readily hydrated by this ***fungal*** epoxide hydrase showing that it has a stringent substrate specificity. Anal. of the enzymic hydration product on boric acid-impregnated silica gel plates showed that the product obtained from the cis epoxide was exclusively erythro while acid hydrolysis of this epoxide gave rise to the expected threo product. This enzyme is novel in that it catalyzes cis hydration of epoxide while the

other epoxide hydrases heretofore isolated catalyzed trans hydration of epoxides.

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=> E ARAND/AU
=> S E18,E19,E21,E22
            16 "ARAND M"/AU
             1 "ARAND M E"/AU
            59 "ARAND MICHAEL"/AU
             1 "ARAND MICHAEL E"/AU
L12         76 ("ARAND M"/AU OR "ARAND M E"/AU OR "ARAND MICHAEL"/AU OR "ARAND
               MICHAEL E"/AU)

=> E ARCHELAS/AU
=> S E4-E6
            34 "ARCHELAS A"/AU
            33 "ARCHELAS ALAIN"/AU
             1 "ARCHELAS ALAIN ROBERT"/AU
L13         68 ("ARCHELAS A"/AU OR "ARCHELAS ALAIN"/AU OR "ARCHELAS ALAIN ROBER
               T"/AU)

=> E BARATTI/AU
=> S E14-E17
            68 "BARATTI J"/AU
            10 "BARATTI J C"/AU
            17 "BARATTI JACQUES"/AU
            27 "BARATTI JACQUES C"/AU
L14        122 ("BARATTI J"/AU OR "BARATTI J C"/AU OR "BARATTI JACQUES"/AU OR
               "BARATTI JACQUES C"/AU)

=> E FURSTOSS/AU
=> S E9-E11
            53 "FURSTOSS R"/AU
             1 "FURSTOSS R J"/AU
            67 "FURSTOSS ROLAND"/AU
L15        121 ("FURSTOSS R"/AU OR "FURSTOSS R J"/AU OR "FURSTOSS ROLAND"/AU)

=> S L12,L13,L14,L15
L16        307 (L12 OR L13 OR L14 OR L15)

=> S L16 AND L3
L17         73 L16 AND L3

=> S L17 NOT L10
L18         47 L17 NOT L10

=> S L18 NOT L11
L19         43 L18 NOT L11

=> D 1-43 CBIB ABS

L19  ANSWER 1 OF 43  CAPLUS  COPYRIGHT 2004 ACS on STN
2003:968319  The Telltale Structures of  ***Epoxide***  ***Hydrolases***  .
      ***Arand, Michael***  ; Cronin, Annette; Oesch, Franz; Mowbray, Sherry L.;
     Alwyn Jones, T. (Institute of Pharmacology and Toxicology, University of
     Wuerzburg, Wuerzburg, Germany).  Drug Metabolism Reviews, 35(4), 365-383
     (English) 2003.  CODEN: DMTRAR.  ISSN: 0360-2532.  Publisher: Marcel
     Dekker, Inc..
AB   Traditionally,  ***epoxide***  ***hydrolases***  (EH) have been
     regarded as xenobiotic-metabolizing enzymes implicated in the
     detoxification of foreign compds.  They are known to play a key role in
     the control of potentially genotoxic epoxides that arise during metab. of
     many lipophilic compds.  Although this is apparently the main function for
     the mammalian microsomal  ***epoxide***  ***hydrolase***  (mEH),
     evidence is now accumulating that the mammalian sol.  ***epoxide***
      ***hydrolase***  (sEH), despite its proven role in xenobiotic metab.,
     also has a central role in the formation and breakdown of physiol.
     signaling mols.  In addn., a certain class of microbial  ***epoxide***
      ***hydrolases***  has recently been identified that is an integral part
     of a catabolic pathway, allowing the use of specific terpens as sole
     carbon sources.  The recently available x-ray structures of a no. of EHs
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mirror their resp. functions: the microbial terpen EH differs in its fold from the canonical .alpha./.beta. hydrolase fold of the xenobiotic-metabolizing mammalian EHs. It appears that the latter fold is the perfect soln. for the efficient detoxification of a large variety of structurally different epoxides by a single enzyme, whereas the smaller microbial EH, which has a particularly high turnover no. with its prefered substrate, seems to be the better soln. for the hydrolysis of one specific substrate. The structure of the sEH also includes an addnl. catalytic domain that has recently been shown to possess phosphatase activity. Although the physiol. substrate for this second active site has not been identified so far, the majority of known phosphatases are involved in signaling processes, suggesting that the sEH phosphatase domain also has a role in the regulation of physiol. functions.

L19 ANSWER 2 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
2003:462744 The membrane anchor of microsomal ***epoxide*** ***hydrolase*** from human, rat, and rabbit displays an unexpected membrane topology [Erratum to document cited in CA127:216982]. Holler, Romy; ***Arand, Michael*** ; Mecky, Astrid; Oesch, Franz; Friedberg, Thomas (Institute of Toxicology, University of Mainz, Mainz, D-55131, Germany). Biochemical and Biophysical Research Communications, 306(3), 797 (English) 2003. CODEN: BBRCA9. ISSN: 0006-291X. Publisher: Elsevier Science.
AB An erratum.

L19 ANSWER 3 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
2003:421867 Document No. 139:193448 Structure of Rhodococcus erythropolis limonene-1,2- ***epoxide*** ***hydrolase*** reveals a novel active site. ***Arand, Michael*** ; Hallberg, B. Martin; Zou, Jinyu; Bergfors, Terese; Oesch, Franz; Van Der Werf, Mariet J.; De Bont, Jan A. M.; Jones, T. Alwyn; Mowbray, Sherry L. (Department of Toxicology, University of Wuerzburg, Wuerzburg, D-97078, Germany). EMBO Journal, 22(11), 2583-2592 (English) 2003. CODEN: EMJODG. ISSN: 0261-4189. Publisher: Oxford University Press.
AB ***Epoxide*** ***hydrolases*** are essential for the processing of epoxide-contg. compds. in detoxification or metab. The classic ***epoxide*** ***hydrolases*** have an .alpha./.beta. hydrolase fold and act via a two-step reaction mechanism including an enzyme-substrate intermediate. We report here the structure of the limonene-1,2- ***epoxide*** ***hydrolase*** from Rhodococcus erythropolis, solved using single-wavelength anomalous dispersion from a selenomethionine-substituted protein and refined at 1.2 .ANG. resoln. This enzyme represents a completely different structure and a novel one-step mechanism. The fold features a highly curved six-stranded mixed .beta.-sheet, with four .alpha.-helixes packed onto it to create a deep pocket. Although most residues lining this pocket are hydrophobic, a cluster of polar groups, including an Asp-Arg-Asp triad, interact at its deepest point. Site-directed mutagenesis supports the conclusion that this is the active site. Further, a 1.7 .ANG. resoln. structure shows the inhibitor valpromide bound at this position, with its polar atoms interacting directly with the residues of the triad. We suggest that several bacterial proteins of currently unknown function will share this structure and, in some cases, catalytic properties.

L19 ANSWER 4 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
2003:155750 Document No. 138:398062 The N-terminal domain of mammalian soluble ***epoxide*** ***hydrolase*** is a phosphatase. Cronin, Annette; Mowbray, Sherry; Durk, Heike; Homburg, Shirli; Fleming, Ingrid; Fisslthaler, Beate; Oesch, Franz; ***Arand, Michael*** (Institute of Pharmacology and Toxicology, University of Wurzburg, Wurzburg, D-97078, Germany). Proceedings of the National Academy of Sciences of the United States of America, 100(4), 1552-1557 (English) 2003. CODEN: PNASA6. ISSN: 0027-8424. Publisher: National Academy of Sciences.
AB The mammalian sol. ***epoxide*** ***hydrolase*** (sEH) is an enzyme with multiple functions, being implicated in detoxification of xenobiotic epoxides as well as in regulation of physiol. processes such as blood pressure. The enzyme is a homodimer, in which each subunit is composed of two domains. The 35-kDa C-terminal domain has an .alpha./.beta. hydrolase fold and harbors the catalytic center for the EH activity. The 25-kDa N-terminal domain has a different .alpha./.beta. fold and belongs to the haloacid dehalogenase superfamily of enzymes. The

catalytic properties of the enzyme reported so far can all be explained by the action of the C-terminal domain alone. The function of the N-terminal domain, other than in structural stabilization of the dimer, has therefore remained unclear. By structural comparison of this domain to other haloacid dehalogenase family members, we identified a putative active site contg. all necessary components for phosphatase activity. Subsequently, we found rat sEH hydrolyzed 4-nitrophenyl phosphate with a rate const. of 0.8 s-1 and a Km of 0.24 mM. Recombinant human sEH lacking the C-terminal domain also displayed phosphatase activity. Presence of a phosphatase substrate did not affect epoxide turnover nor did epoxides affect dephosphorylation by the intact enzyme, indicating both catalytic sites act independently. The enzyme was unable to hydrolyze 4-nitrophenyl sulfate, suggesting its role in xenobiotic metab. does not extend beyond phosphates. Thus, we propose this domain participates instead in the regulation of the physiol. functions assocd. with sEH.

L19 ANSWER 5 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
2002:917933 Document No. 139:80552 Interest of genotyping and phenotyping of drug-metabolizing enzymes for the interpretation of biological monitoring of exposure to styrene. Haufroid, Vincent; Jakubowski, Marek; Janasik, Beata; Ligocka, Danuta; Buchet, Jean-Pierre; Bergamaschi, Enrico; Manini, Paola; Mutti, Antonio; Ghittori, Sergio; ***Arand, Michael*** ; Hangen, Nina; Oesch, Franz; Hirvonen, Ari; Lison, Dominique (Industrial Toxicology and Occupational Medicine Unit, Catholic University of Louvain, Brussels, B-1200, Belg.). Pharmacogenetics, 12(9), 691-702 (English) 2002. CODEN: PHMCEE. ISSN: 0960-314X. Publisher: Lippincott Williams & Wilkins.
AB In the field of occupational and/or environmental toxicol., the measurement of specific metabolites in urine may serve to assess exposure to the parent compds. (biol. monitoring of exposure). Styrene is one of the chems. for which biol. monitoring programs have been validated and implemented in environmental and occupational medicine. However, inter-individual differences in the urinary excretion exist both for the main end-products (mandelic acid and phenylglyoxylic acid) and for its specific mercapturic acids (phenylhydroxyethylmercapturic acids, PHEMA). This limits to a certain extent the use of these metabolites for an accurate assessment of styrene exposure. In a group of 26 volunteers selected with relevant genotypes, and exposed to styrene vapors (50 mg/m , 8 h) in an inhalation chamber, the authors evaluated whether genotyping or phenotyping relevant drug-metabolizing enzymes (CYP2E1, EPHX1, GSTM1, GSTT1 and GSTP1) may help to explain the obsd. inter-individual variability in the urinary metabolite excretion. Peripheral blood lymphocytes were used for genotyping and as reporter cells for the phenotyping of CYP2E1 and EPHX1. The genotype was clearly the most significant parameter explaining the variance in urinary PHEMA excretion (6-fold lower in null subjects; 0.0001) so that systematic genotyping should be recommended routinely for a correct interpretation of PHEMA urinary levels. Variant alleles (7632T A) and were assocd. with a significant redn. of, resp., the expression (= 0.047) and activity (= 0.022) of the enzyme in peripheral blood lymphocytes. In combination with genotyping, the phenotyping approach also contributed to improve the interpretation of urinary results, as illustrated by the combined effect of CYP2E1 expression and allelic status that explained 77% of the variance in PHEMA excretion and allows the recommendation of mercapturates as specific and reliable biomarkers of exposure to styrene.

L19 ANSWER 6 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
2002:858579 Document No. 138:165609 Biocatalytic potential of the ***epoxide*** ***hydrolase*** from Agrobacterium radiobacter AD1 and a mutant with enhanced enantioselectivity. Spelberg, Jeffrey H. Lutje; Rink, Rick; ***Archelas, Alain*** ; ***Furstoss, Roland*** ; Janssen, Dick B. (Department of Biochemistry, Groningen Biomolecular Sciences and Biotechnology Institute, Groningen, 9747 AG, Neth.). Advanced Synthesis & Catalysis, 344(9), 980-985 (English) 2002. CODEN: ASCAF7. ISSN: 1615-4150. Publisher: Wiley-VCH Verlag GmbH & Co. KGaA.
AB Optically pure epoxides are useful synthons for a variety of biol. active compds. The ***epoxide*** ***hydrolase*** obtained from Agrobacterium radiobacter AD1 hydrolyzes racemic aryl epoxides with moderate and aliph. epoxides with low enantioselectivity. The three-dimensional structure of this enzyme indicates that two tyrosine residues interact with the epoxide oxygen. Mutating one of these, tyrosine 215, to a phenylalanine (Y215F) resulted in an enzyme with

increased enantioselectivity towards aryl epoxides. The relatively strong decrease in activity towards the remaining enantiomers makes this enzyme a much better biocatalyst than the wild-type enzyme for the prepn. of optically pure (S)-styrene oxide derivs.

L19 ANSWER 7 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
2002:795661 Document No. 138:85503 Stereochemical features of the hydrolysis of 9,10-epoxystearic acid catalysed by plant and mammalian ***epoxide*** ***hydrolases*** . Summerer, Stephan; Hanano, Abdulsamie; Utsumi, Shigeru; ***Arand, Michael*** ; Schuber, Francis; Blee, Elizabeth (Laboratoire des Phytooxylipines, IBMP-CNRS-UPR 2357, Strasbourg, 67 083, Fr.). Biochemical Journal, 366(2), 471-480 (English) 2002. CODEN: BIJOAK. ISSN: 0264-6021. Publisher: Portland Press Ltd..
AB Cis-9,10-Epoxystearic acid was used as a tool to probe the active sites of ***epoxide*** ***hydrolases*** (EHs) of mammalian and plant origin. We have compared the stereochem. features of the hydrolysis of this substrate catalyzed by sol. and membrane-bound rat liver EHs, by sol. EH (purified to apparent homogeneity) obtained from maize seedlings or celeriac roots, and by recombinant soybean EH expressed in yeast. Plant EHs were found to differ in their enantioselectivity, i.e. their ability to discriminate between the two enantiomers of 9,10-epoxystearic acid. For example, while the maize enzyme hydrated both enantiomers at the same rate, the EH from soybean exhibited very high enantioselectivity in favor of 9R,10S-epoxystearic acid. This latter enzyme also exhibited a strict stereoselectivity, i.e. it hydrolyzed the racemic substrate with a very high enantioconvergence, yielding a single chiral diol product, threo-9R,10R-dihydroxystearic acid. Soybean EH shared these distinctive stereochem. features with the membrane-bound rat liver EH. The stereochem. outcome of these enzymes probably results from a stereoselective attack by the nucleophilic residue on the oxirane ring carbon having the (S)-configuration, leading to the presumed (in plant EH) covalent acyl-enzyme intermediate. In sharp contrast, the reactions catalyzed by cytosolic rat liver EH exhibited a complete absence of enantioselectivity and enantioconvergence; this latter effect might be ascribed to a regioselective formation of the acyl-enzyme intermediate involving C-10 of 9,10-epoxystearic acid, independent of its configuration. Thus, compared with soybean EH, the active site of rat liver sol. EH displays a very distinct means of anchoring the oxirane ring of the fatty acid epoxides, and therefore appears to be a poor model for mapping the catalytic domain of plant EHs.

L19 ANSWER 8 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
2002:375169 Document No. 137:165400 Sequestration of biological reactive intermediates by trapping as covalent enzyme-intermediate complex. Oesch, Franz; Herrero, Maria Elena; Lohmann, Matthias; Hengstler, Jan Georg; ***Arand, Michael*** (Institute of Toxicology, University of Mainz, Mainz, D-55131, Germany). Advances in Experimental Medicine and Biology, 500(Biological Reactive Intermediates VI), 577-586 (English) 2001. CODEN: AEMBAP. ISSN: 0065-2598. Publisher: Kluwer Academic/Plenum Publishers.
AB One important class of biol. reactive intermediates arising in the course of human xenobiotic metab. are arene and alkene oxides. The major safeguard against the potential genotoxic effects of these compds. is the microsomal ***epoxide*** ***hydrolase*** (mEH). This enzyme has a broad substrate specificity but - on the first sight - seems to be inadequately suited for this protection task due to its low turnover no. with most of its substrates. The recent progress in the understanding of the mechanism of enzymic epoxide hydrolysis has shed new light on this apparent dilemma: ***Epoxide*** ***hydrolases*** convert their substrates via the intermediate formation of a covalent enzyme-substrate complex, and it has been shown that the formation of the intermediate proceeds by orders of magnitudes faster than the subsequent hydrolysis, i.e. the formation of the terminal product. Thus, the enzyme acts like a mol. sponge by binding and inactivating the dangerous metabolite very fast while the subsequent product release is considerably slower, and quantification of the latter heavily underestimates the speed of detoxification. Usually, the slow enzyme regeneration does not pose a problem, since the mEH is highly abundant in human liver, the organ with the highest capacity to metabolically generate epoxides. Computer simulation provides evidence that the high amt. of mEH enzyme is crucial for the control of the steady-state level of a substrate epoxide and can keep it extremely low. Once the mEH is titrated out under conditions of

extraordinarily high epoxide concn., the epoxide steady-state level steeply rises, leading to a sudden burst of the genotoxic effect. This prediction of the computer simulation is in perfect agreement with our exptl. work. V79 Chinese Hamster cells that we have genetically engineered to express human mEH at about the same level as that obsd. in human liver are well protected from any measurable genotoxic effect of the model compd. styrene oxide (STO) up to an apparent threshold level of 100 .mu.M in the cell culture medium. In V79 cells that do not express mEH, STO triggers the formation of DNA strand breaks in a dose-dependent manner with no apparent threshold. Above 100 .mu.M, the genotoxic effect of STO in the mEH-expressing cell line parallels the one in the parental cell line.

L19 ANSWER 9 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
2001:321711 Document No. 134:325230 Synthetic applications of ***epoxide*** ***hydrolases*** . ***Archelas, Alain*** ; ***Furstoss, Roland*** (Groupe Biocatalyse et Chimie Fine, UMR CNRS 6111, Universite de la Mediterranee, Faculte des Sciences de Luminy, Marseille, 13288, Fr.). Current Opinion in Chemical Biology, 5(2), 112-119 (English) 2001. CODEN: COCBF4. ISSN: 1367-5931. Publisher: Elsevier Science Ltd..
AB A review with 58 refs. There have been several recent advances in the area of biocatalyzed hydrolytic kinetic resoln. of epoxides using "newly discovered" enzymes (i.e. ***epoxide*** ***hydrolases***). These biocatalysts, two of which will become com. available in the near future, appear to be highly promising tools for fine org. synthesis, as they enable the prepn. of various epoxides and/or their corresponding diols in enantiopure form.

L19 ANSWER 10 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
2001:222367 Document No. 135:76732 Microbiological transformations. Part 48: Enantioselective biohydrolysis of 2-, 3- and 4-pyridyloxirane at high substrate concentration using the Agrobacterium radiobacter AD1 ***epoxide*** ***hydrolase*** and its Tyr215Phe mutant. Genzel, Y.; ***Archelas, A.*** ; Lutje Spelberg, J. H.; Janssen, D. B.; ***Furstoss, R.*** (Groupe Biocatalyse et Chimie Fine, Faculte des Sciences de Luminy, Universite de la Mediterranee, UMR CNRS 6111, Marseille, 13288, Fr.). Tetrahedron, 57(14), 2775-2779 (English) 2001. CODEN: TETRAB. ISSN: 0040-4020. OTHER SOURCES: CASREACT 135:76732. Publisher: Elsevier Science Ltd..
AB The ***epoxide*** ***hydrolase*** (EH) from Agrobacterium radiobacter AD1 wild type (ArWT) and its Tyr215Phe mutant were compared for the biocatalyzed hydrolytic kinetic resoln. (BHKR) of 2-, 3- and 4-pyridyloxirane. The regioselectivity of the oxirane ring opening as well as the substrate concn. limit and the inhibitory effect of the diol were detd. A gram scale prepn. of enantiopure 2-pyridyloxirane (enantiomeric excess > 98%) at a concn. as high as 127 mM (15.5 g/L) could be achieved with each of these two enzymes.

L19 ANSWER 11 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
2001:47555 Document No. 134:295582 Microbiological transformations. Part 45: A green chemistry preparative scale synthesis of enantiopure building blocks of Eliprodil: elaboration of a high substrate concentration ***epoxide*** ***hydrolase*** -catalyzed hydrolytic kinetic resolution process. Manoj, K. M.; ***Archelas, A.*** ; ***Baratti,*** *** J.*** ; ***Furstoss, R.*** (Group Biocatalyse et Chemie Fine, Faculte de Sciences de Luminy, ESA 6111 Associee au CNRS, University of Mediterranee, Marseille, 13288, Fr.). Tetrahedron, 57(4), 695-701 (English) 2001. CODEN: TETRAB. ISSN: 0040-4020. OTHER SOURCES: CASREACT 134:295582. Publisher: Elsevier Science Ltd..
AB The enantioselective hydrolysis of racemic p-chlorostyrene oxide (I) following a typical green chem. procedure based on the use of two different ***epoxide*** ***hydrolases*** is described. This allows the prepn. of both enantiomers of I in very high enantiomeric purity. Furthermore, using a one-pot sequential bi-enzymic strategy enabling to overcome the 50% yield limitation intrinsic to any resoln. process, rac-I could be transformed into nearly enantiopure (R)-4-ClC6H4CH(OH)CH2OH with an overall yield as high as 93%. The methodol. developed was based on the use of a biphasic reactor at high substrate concn., which is highly desirable for any potential industrial process. The obtained chirons are valuable building blocks for the

synthesis of various biol. active targets, like (R)-Eliprodil.

L19 ANSWER 12 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
2000:430960 Document No. 133:248221 Metabolic detoxification: Implications for thresholds. Oesch, Franz; Herrero, Maria Elena; Hengstler, Jan Georg; Lohmann, Matthias; ***Arand, Michael*** (Institute of Toxicology, University of Mainz, Mainz, D-55131, Germany). Toxicologic Pathology, 28(3), 382-387 (English) 2000. CODEN: TOPADD. ISSN: 0192-6233. Publisher: Society of Toxicologic Pathologists.
AB The fact that chem. carcinogenesis involves single, isolated, essentially irreversible mol. events as discrete steps, several of which must occur in a row to finally culminate in the development of a malignancy, rather suggests that an abs. threshold for chem. carcinogens may not exist. However, practical thresholds may exist due to saturable pathways involved in the metabolic processing, esp. in the metabolic inactivation, of such compds. An important example for such a pathway is the enzymic hydrolysis of epoxides via ***epoxide*** ***hydrolases*** , a group of enzymes for which the catalytic mechanism has recently been established. These enzymes convert their substrates via the intermediate formation of a covalent enzyme-substrate complex. Interestingly, the formation of the intermediate proceeds faster by orders of magnitude than the subsequent hydrolysis, ie, the formation of the terminal product. Under normal circumstances, this does not pose a problem, since the microsomal ***epoxide*** ***hydrolase*** (mEH), the ***epoxide*** ***hydrolases*** with the best documented importance in the metab. of carcinogens, is highly abundant in the liver, the organ with the highest capacity to metabolically generate epoxides. Computer simulation provides evidence that the high amt. of mEH enzyme is favorable for the control of the steady-state level of a substrate epoxide and can keep it extremely low. However, once the mEH is titrated out under conditions of extraordinarily high epoxide concn., the epoxide steady-state level steeply rises, leading to a sudden burst of the genotoxic effect of the noxious agent. This prediction of the computer simulation is nicely supported by exptl. work. V79 Chinese hamster cells that the authors have genetically engineered to express human mEH at about the same level as that obsd. in human liver are completely protected from any measurable genotoxic effect of the model compd. styrene oxide (STO) up to a dose of 100 .mu.M in the cell culture medium (toxicokinetic threshold). In V79 cells that do not express mEH, STO leads to the formation of DNA strand breaks in a dose-dependent manner with no toxicokinetic threshold observable. Above 100 .mu.M, the genotoxic effect of STO in the mEH-expressing cell line parallels the one in the parental cell line. Thus, the saturable protection from STO-induced strand breaks by mEH represents a typical example of a practical threshold. However, it must be pointed out that even in the presence of protective amts. of mEH, a minute but definite level of STO is present that does not contribute sufficiently to the strand break formation to overcome the background noise of the detection procedure. As pointed out above, abs. thresholds probably do not exist in chem. carcinogenesis.

L19 ANSWER 13 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
2000:191865 Document No. 132:320393 Identification of the putative brain tumor antigen BF7/GE2 as the (De)toxifying enzyme microsomal ***epoxide*** ***hydrolase*** . Kessler, Reto; Hamou, Marie-France; Albertoni, Michele; De Tribolet, Nicolas; ***Arand, Michael*** ; Van Meir, Erwin G. (Laboratory of Tumor Biology and Genetics, Neurosurgery Department, University Hospital (CHUV), Lausanne, 1011, Switz.). Cancer Research, 60(5), 1403-1409 (English) 2000. CODEN: CNREA8. ISSN: 0008-5472. Publisher: AACR Subscription Office.
AB Malignant gliomas are the main cause of death from primary brain tumors. Despite surgery, radiation, and chemotherapy, patients have a median survival of less than a few years; therefore, it is clearly imperative to investigate new ways of treatment. The development of new therapeutic strategies for brain tumors is dependent on a better understanding of the differences between normal and tumoral brain cells. Our group had described previously a Mr 48,000 antigen defined by reactivity with two monoclonal antibodies (GE2 and BF7) obtained by immunization of mice with human glioblastoma cells. Here, we describe the identification of the GE2/BF7 antigen as microsomal ***epoxide*** ***hydrolase*** (mEH), a drug-metabolizing enzyme that is involved both in toxification and detoxification of carcinogens. We initially used immunoaffinity purifn.

using GE2 and BF7 and analyzed the purified proteins by microsequencing. Edman degrdn. identified 15 amino acids of the NH2-terminal sequence that were 100% identical to mEH. To further confirm the identity of the BF7/GE2 antigen as mEH, we showed that the protein immunopurified with GE2 and BF7 was recognized by an anti-mEH antibody and that in vitro and in vivo synthesized human mEH is recognized by BF7 and GE2 antibodies. Furthermore, anti-mEH antibody recognizes an antigen expressed both in gliomas and reactive astrocytes, as do BF7 and GE2. Finally, we demonstrate that in contrast to what has been reported in rat embryo fibroblasts, p53 does not regulate mEH mRNA expression in glioma cells.

L19 ANSWER 14 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
2000:143187 Document No. 133:27396 Role of individual enzymes in the control of genotoxic metabolites. Oesch, Franz; ***Arand, Michael*** (Institute of Toxicology, University of Mainz, Mainz, D-55131, Germany). NATO ASI Series, Series A: Life Sciences, 303(Molecular and Applied Aspects of Oxidative Drug Metabolizing Enzymes), 211-220 (English) 1999. CODEN: NALSDJ. ISSN: 0258-1213. Publisher: Kluwer Academic/Plenum Publishers.
AB A review with 17 refs. is given on the phase concept of xenobiotic metab., enzymes implicated in xenobiotic metab., the metab. of benzo[A]pyrene, the metab. of chrysene diol epoxide isomers by mammalian ***epoxide*** ***hydrolases*** , and activation of aliph. carcinogens.

L19 ANSWER 15 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
1999:770362 Document No. 132:166400 Transketolase-mediated synthesis of 4-deoxy-D-fructose 6-phosphate by ***epoxide*** - ***hydrolase*** -catalysed resolution of 1,1-diethoxy-3,4-epoxybutane. Guerard, Christine; Alphand, Veronique; ***Archelas, Alain*** ; Demuynck, Colette; Hecquet, Laurence; ***Furstoss, Roland*** ; Bolte, Jean (Dep. Chimie, Lab. SEESIB, Univ. Blaise-Pascal, Aubiere, F-63177, Fr.). European Journal of Organic Chemistry (12), 3399-3402 (English) 1999. CODEN: EJOCFK. ISSN: 1434-193X. OTHER SOURCES: CASREACT 132:166400. Publisher: Wiley-VCH Verlag GmbH.
AB 4-Deoxy-D-fructose 6-phosphate is synthesized from nonnatural sources in 4 steps, including 2 enzymic reactions. (3S)-1,1-diethoxy-3,4-epoxybutane is first obtained by ***epoxide*** - ***hydrolase*** -catalyzed resoln. Opening of this epoxide by inorg. phosphate leads to 2-deoxy-D-erythrose 4-phosphate. In the last step, transketolase transfers a hydroxyacetyl group from L-erythrulose onto this aldehyde, controlling the second asym. center.

L19 ANSWER 16 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
1999:436701 Document No. 131:228314 Absolute Configuration of .alpha.-Methylstyrene Oxide: The Correct Absolute Configuration/Optical Rotation Correlation. ***Archelas, A.*** ; ***Furstoss, R.*** (Groupe Biocatalyse et Chimie Fine, ESA 6111 associee au CNRS Faculte des Sciences de Luminy, Marseille, 13288, Fr.). Journal of Organic Chemistry, 64(16), 6112-6114 (English) 1999. CODEN: JOCEAH. ISSN: 0022-3263. Publisher: American Chemical Society.
AB Using literature data, the authors have unambiguously established the optical rotation/abs. configuration correlation for .alpha.-methylstyrene oxide (I) enantiomers; the sign of this rotation depends on the solvent used to achieve this measurement. The biocatalysis of I using either A. niger or A. radiobacter ***epoxide*** ***hydrolases*** , were enantiocomplementary, thus allowing prepn. of both enantiomers of I, at will, by choosing the appropriate biocatalyst.

L19 ANSWER 17 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
1999:167185 Document No. 130:334420 Differential subcellular localization of endogenous and transfected soluble ***epoxide*** ***hydrolase*** in mammalian cells: evidence for isoenzyme variants. Mullen, Robert T.; Trelease, Richard N.; Duerk, Heike; ***Arand, Michael*** ; Hammock, Bruce D.; Oesch, Franz; Grant, David F. (Department of Plant Biology, Arizona State University, Tempe, AZ, 85287-1601, USA). FEBS Letters, 445(2,3), 301-305 (English) 1999. CODEN: FEBLAL. ISSN: 0014-5793. Publisher: Elsevier Science B.V..
AB Endogenous, constitutive sol. ***epoxide*** ***hydrolase*** in mice 3T3 cells was localized via immunofluorescence microscopy exclusively in peroxisomes, whereas transiently expressed mouse sol. ***epoxide*** ***hydrolase*** (from clofibrate-treated liver) accumulated only in the

cytosol of 3T3 and HeLa cells. When the C-terminal Ile of mouse sol. ***epoxide*** ***hydrolase*** was mutated to generate a prototypic putative type 1 PTS (-SKI to -SKL), the enzyme targeted to peroxisomes. The possibility that sol. ***epoxide*** ***hydrolase*** -SKI was sorted slowly to peroxisomes from the cytosol was examd. by stably expressing rat sol. ***epoxide*** ***hydrolase*** -SKI appended to the green fluorescent protein. Green fluorescent protein sol. ***epoxide*** ***hydrolase*** -SKI was strictly cytosolic, indicating that -SKI was not a temporally inefficient putative type 1 PTS. Import of sol. ***epoxide*** ***hydrolase*** -SKI into peroxisomes in plant cells revealed that the context of -SKI on sol. ***epoxide*** ***hydrolase*** was targeting permissible. These results show that the C-terminal -SKI is a non-functional putative type 1 PTS on sol. ***epoxide*** ***hydrolase*** and suggest the existence of distinct cytosolic and peroxisomal targeting variants of sol. ***epoxide*** ***hydrolase*** in mouse and rat.

L19 ANSWER 18 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN

1999:37265 Document No. 130:193575 Catalytic triad of microsomal ***epoxide*** ***hydrolase*** : replacement of Glu404 with Asp leads to a strongly increased turnover rate. ***Arand, Michael*** ; Muller, Frank; Mecky, Astrid; Hinz, Willy; Urban, Phillipe; Pompon, Denis; Kellner, Roland; Oesch, Franz (Institute of Toxicology, University of Mainz, Mainz, D-55131, Germany). Biochemical Journal, 337(1), 37-43 (English) 1999. CODEN: BIJOAK. ISSN: 0264-6021. Publisher: Portland Press Ltd..

AB Microsomal ***epoxide*** ***hydrolase*** (mEH) belongs to the superfamily of .alpha./.beta.-hydrolase fold enzymes. A catalytic triad in the active center of the enzyme hydrolyzes the substrate mols. in a 2-step reaction via the intermediate formation of an enzyme-substrate ester. Here, the authors show that the mEH catalytic triad comprises Asp-226, Glu-404, and His-431. Replacing either of these residues with nonfunctional amino acids results in a complete loss of activity of the enzyme recombinantly expressed in Saccharomyces cerevisiae. For Glu-404 and His-431 mutants, their structural integrity was demonstrated by their retained ability to form the substrate ester intermediate, indicating that the lack of enzymic activity is due to an indispensable function of either residue in the hydrolytic step of the enzymic reaction. The role of Asp-226 as the catalytic nucleophile driving the formation of the ester intermediate was substantiated by the isolation of a peptide fraction carrying the 14C-labeled substrate after cleavage of the ester intermediate with CNBr. Sequence anal. revealed that 1 of the 2 peptides within this sample harbored Asp-226. Surprisingly, the replacement of Glu-404 with Asp greatly increased the Vmax of the enzyme with styrene 7,8-oxide (23-fold) and 9,10-epoxystearic acid (39-fold). The increase in Vmax was paralleled by an increase in Km with both substrates, in line with a selective enhancement of the 2nd, rate-limiting step of the enzymic reaction. Owing to its enhanced catalytic properties, the E404D mutant might represent a versatile tool for the enantioselective bioorg. synthesis of chiral fine chems. The question of why all native mEHs analyzed so far have a Glu in place of the acidic charge relay residue is discussed.

L19 ANSWER 19 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN

1998:698813 Document No. 130:108248 Polymorphisms of N-acetyltransferases, glutathione S-transferases, microsomal ***epoxide*** ***hydrolase*** and sulfotransferases: influence on cancer susceptibility. Hengstler, J. G.; ***Arand, M.*** ; Herrero, M. E.; Oesch, F. (Institute of Toxicology, Mainz, 55131, Germany). Recent Results in Cancer Research, 154(Genes and Environment in Cancer), 47-85 (English) 1998. CODEN: RRCRBU. ISSN: 0080-0015. Publisher: Springer-Verlag.

AB A review, with many refs. It has become clear that several polymorphisms of human drug-metabolizing enzymes influence an individual's susceptibility for chem. carcinogenesis. This review gives an overview on relevant polymorphisms of four families of drug-metabolizing enzymes. Rapid acetylators (with respect to N-acetyltransferase NAT2) were shown to have an increased risk of colon cancer, but a decreased risk of bladder cancer. In addn. an assocn. between a NAT1 variant allele (NAT*10, due to mutations in the polyadenylation site causing .apprx.2-fold higher activity) and colorectal cancer among NAT2 rapid acetylators was obsd., suggesting a possible interaction between NAT1 and NAT2. Glutathione

S-transferases M1 and T1 (GSTM1 and GSTT1) are polymorphic due to large deletions in the structural gene. Meta-anal. of 12 case-control studies demonstrated a significant assocn. between the homozygous deletion of GSTM1 (GSTM1-0) and lung cancer. Combination of GSTM1-0 with two allelic variants of cytochrome P 450 1A1 (CYP1A1), CYP1A1 m2/m2 and CYP1A1 Val/Val further increases the risk for lung cancer. Indirect mechanisms by which deletion of GSTM1 increases risk for lung cancer may include GSTM1-0 assocd. decreased expression of GST M3 and increased activity of CYP1A1 and 1A2. Combination of GST M1-0 and NAT2 slow acetylation was assocd. with markedly increased risk for lung cancer. In addn. GSTM1-0 is clearly assocd. with bladder cancer and possibly also with colorectal, hepatocellular, gastric, esophageal (interaction with CYP1A1), head and neck as well as cutaneous cancer. In individuals with the GSTT1-0 genotype more chromosomal aberrations and sister chromatid exchanges (SCEs) were obsd. after exposure to 1,3-butadiene or various haloalkanes or haloalkenes. Evidence for an assocn. between GSTT1-0 and myelodysplastic syndrome and acute lymphoblastic leukemia has been presented. A polymorphic site of GSTP1 (valine to isoleucine at codon 104) decreases activity to several carcinogenic diol epoxides and was assocd. with testicular, bladder and lung cancer. Microsomal expoxide hydrolase (mEH) is polymorphic due to amino acid variation at residues 113 and 139. Polymorphic variants of mEH were assocd. with hepatocellular cancer (His-113 allele), ovarian cancer (Tyr-113 allele) and chronic obstructive pulmonary disease (His-113 allele). Three human sulfotransferases (STs) are regulated by genetic polymorphisms (hDHEAST, hM-PST, TS PST). Since a large no. of environmental mutagens are activated by STs an assocn. with human cancer risk might be expected.

L19 ANSWER 20 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
1998:533877 Document No. 129:260283 Determination of the regioselectivity during ***epoxide*** ***hydrolase*** oxirane ring opening: a new method from racemic epoxides. Moussou, Philippe; ***Archelas, Alain*** ; ***Baratti, Jacques*** ; ***Furstoss, Roland*** (Faculte des Sciences de Luminy, ERS CNRS 157, Groupe Biocatalyse et Chimie Fine, Universite de la Mediterranee, Marseille, 13288, Fr.). Journal of Molecular Catalysis B: Enzymatic, 5(1-4), 213-217 (English) 1998. CODEN: JMCEF8. ISSN: 1381-1177. Publisher: Elsevier Science B.V..
AB We describe here a new method for the detn. of the regioselectivity of oxirane ring opening involved in ***epoxide*** ***hydrolase*** catalyzed hydrolysis of epoxides, simply by starting from the racemic epoxide as substrate. This method permits simultaneous detn. of the enantioselectivity (E) ratio according to Sih's equation, the applicability of which in this context is discussed. This approach affords a complete characterization of the biocatalyzed epoxide opening, where three different stereochem. behaviors can be distinguished.

L19 ANSWER 21 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
1998:363427 Document No. 129:95124 Microbiological transformations. Part 39: Determination of the regioselectivity occurring during oxirane ring opening by ***epoxide*** ***hydrolases*** : a theoretical analysis and a new method for its determination. Moussou, Philippe; ***Archelas,*** *** Alain*** ; ***Baratti, Jacques*** ; ***Furstoss, Roland*** (Groupe Biocatalyse et Chimie Fine, ERS 157 associee au CNRS, Faculte des Sciences de Luminy, Marseille, 13288, Fr.). Tetrahedron: Asymmetry, 9(9), 1539-1547 (English) 1998. CODEN: TASYE3. ISSN: 0957-4166. OTHER SOURCES: CASREACT 129:95124. Publisher: Elsevier Science Ltd..
AB New equations as well as a new method were devised allowing for the total detn. of the regioselectivity of biohydrolysis of a racemic epoxide by an ***epoxide*** ***hydrolase*** . This detn. is achievable by simply studying the racemic epoxide as a substrate. Depending on the enantioselectivity (E value) and the regioselectivity involved, the abs. configuration as well as the enantiopurity of the residual epoxide and of the formed diol appear to be highly variable. For a specific enzyme/substrate couple, the yield and enantiopurity of the less reactive (remaining) epoxide - and thus the possibility to prep. it in enantiopure form - exclusively depend upon the enzyme enantioselectivity. On the other hand, the ee of the formed diol depends upon the enantioselectivity and regioselectivity of the oxirane ring opening. A theor. anal. based on the material balance, as well as several practical examples, are provided to illustrate the various possibilities of such biohydrolysis.

L19 ANSWER 22 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
1998:191502 Document No. 129:1961 ***Epoxide*** ***hydrolases*** : new tools for the synthesis of fine organic chemicals. ***Archelas,*** *** Alain*** ; ***Furstoss, Roland*** (Groupe Biocatalyse Chimie Fine, ERS 157 CNRS, Univ. La Mediterranee, Fac. Sci. Luminy, Marseille, 13288, Fr.). Trends in Biotechnology, 16(3), 108-116 (English) 1998. CODEN: TRBIDM. ISSN: 0167-7799. Publisher: Elsevier Science Ltd..
AB A review, with 71 refs. ***Epoxide*** ***hydrolases*** are ubiquitous enzymes able to hydrolyze an epoxide to its corresponding vicinal diol. These hydrolases have been shown often to be highly enantio- and regioselective, thus allowing both the epoxide and the diol to be prepd. at high enantiomeric purity. Because these products show high chem. versatility, they are important for the synthesis of various biol. active products. Recent studies have provided valuable information on the mol. structure of these enzymes, as well as insight to the enzymic mechanisms involved.

L19 ANSWER 23 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
1998:20778 Document No. 128:124741 Recombinant expression of human microsomal ***epoxide*** ***hydrolase*** protects V79 Chinese Hamster cells from styrene oxide- but not from ethylene oxide-induced DNA strand breaks. Herrero, Maria Elena; ***Arand, Michael*** ; Hengstler, Jan Georg; Oesch, Franz (Institute of Toxicology, University of Mainz, Mainz, D-55131, Germany). Environmental and Molecular Mutagenesis, 30(4), 429-439 (English) 1997. CODEN: EMMUEG. ISSN: 0893-6692. Publisher: Wiley-Liss, Inc..
AB In order to study the role of human microsomal ***epoxide*** ***hydrolase*** (hmEH) in protecting cells against genotoxicity of styrene 7,8-oxide and ethylene oxide, we expressed the cDNA of hmEH in V79 Chinese hamster cells. We obtained a no. of cell clones that expressed functionally active ***epoxide*** ***hydrolase*** . Among these, the clone 92hmEH-V79 revealed an esp. high enzymic mEH activity toward styrene 7,8-oxide (10 nmol converted per mg of protein per min, measured in the 9,000 .times. g supernatant of the cell homogenate), that was 100 times higher than that detd. in mock-transfected cells and within the range of mEH activity in human liver. Styrene 7,8-oxide-induced DNA single-strand breaks/alkali labile sites (dose range 10 .mu.M to 1 mM styrene 7,8-oxide) measured by the alk. elution technique were significantly lower in the 92hmEH-V79 cells as compared to the mock-transfected cells. The protection against styrene 7,8-oxide genotoxicity in 92hmEH-V79 cells could be abolished by addn. of valpromide, a selective inhibitor of microsomal ***epoxide*** ***hydrolase*** . These results clearly show that the metab. of styrene 7,8-oxide by hmEH in 92hmEH-V79 cells was responsible for the protection against styrene 7,8-oxide genotoxicity. On the other hand, no protective effect of ***epoxide*** ***hydrolase*** expression could be obsd. on ethylene oxide-induced DNA damage with the recombinant cell line over a dose range of 0.5-2.5 mM ethylene oxide. This selectivity of the protective effect on epoxide genotoxicity thus appears to be an important factor that must be taken into account for the prediction of the genotoxic risk of epoxides themselves or compds. that can be metabolically activated to epoxides.

L19 ANSWER 24 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
1997:506963 Document No. 127:216982 The membrane anchor of microsomal ***epoxide*** ***hydrolase*** from human, rat, and rabbit displays an unexpected membrane topology. Holler, Romy; ***Arand, Michael*** ; Meckey, Astrid; Oesch, Franz; Friedberg, Thomas (Institute Toxicology, University Mainz, Mainz, D-55131, Germany). Biochemical and Biophysical Research Communications, 236(3), 754-759 (English) 1997. CODEN: BBRCA9. ISSN: 0006-291X. Publisher: Academic.
AB The microsomal ***epoxide*** ***hydrolase*** (mEH) and cytochrome P450s catalyze the sequential formation of carcinogenic metabolites. According to one algorithm for predicting the membrane topol. of proteins, the human, the rabbit, and the rat mEH should adopt a type II topol. The type II topol. is also predicted by a recently established neuronal network which is trained to recognize signal peptides with very high accuracy. In contrast to these predictions, on N-glycosylation anal. in a cell-free and in a cellular system indicate that the membrane anchor of human, rat, and rabbit mEH displays a type I topol. This result is correctly predicted by the pos. inside rule in which neg. charged

residues, the distribution of which differs in the mEH membrane anchor of these species, have only a modulating role for the membrane topol. of proteins. However, these results demonstrate that this role is not strong enough to force the mEHs into a type II topol., not even in the case of the rabbit mEH, in which the only pos. charged residue in the C-terminal part of the topogenic sequence is flanked by 5 neg. charged residues.

L19 ANSWER 25 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
1997:294351 Document No. 127:77830 Visualization of a covalent intermediate between microsomal ***epoxide*** ***hydrolase*** , but not cholesterol ***epoxide*** ***hydrolase*** , and their substrates. Muller, Frank; ***Arand, Michael*** ; Frank, Heinz; Seidel, Albrecht; Hinz, Willy; Winkler, Lars; Hanel, Karen; Blee, Elizabeth; Beetham, Jeffrey K.; Hammock, Bruce D.; Oesch, Franz (Inst. Toxicology, Univ. Mainz, Mainz, D-55131, Germany). European Journal of Biochemistry, 245(2), 490-496 (English) 1997. CODEN: EJBCAI. ISSN: 0014-2956. Publisher: Springer.
AB Mammalian sol. and microsomal ***epoxide*** ***hydrolases*** were proposed to belong to the family of .alpha./.beta.-hydrolase-fold enzymes. These enzymes hydrolyze their substrates by a catalytic triad, with the 1st step of the enzymic reaction being the formation of a covalent enzyme-substrate ester. The direct visualization was described of the ester formation between rat microsomal ***epoxide*** ***hydrolase*** and its substrate. Microsomal ***epoxide*** ***hydrolase*** was pptd. with acetone after brief incubation with [1-14C]epoxystearic acid. After denaturing SDS gel electrophoresis the protein-bound radioactivity was detected by fluorog. Pure ***epoxide*** ***hydrolase*** and crude microsomes showed a single radioactive signal of the expected mol. mass that was suppressed by inclusion of the competitive inhibitor 1,1,1-trichloropropene oxide in the incubation mixt. Similarly, 4-fluorochalcone-oxide-sensitive binding of epoxystearic acid to rat sol. ***epoxide*** ***hydrolase*** was demonstrated in rat liver cytosol. Under similar conditions, no covalent binding of [26-14C]cholesterol-5.alpha.,6.alpha.-epoxide to microsomal proteins or solubilized fractions tenfold enriched in cholesterol ***epoxide*** ***hydrolase*** activity was obsd. It was provided definitive proof for the formation of an enzyme-substrate-ester intermediate formed in the course of epoxide hydrolysis by microsomal ***epoxide*** ***hydrolase*** , show no formation of a covalent intermediate between cholesterol ***epoxide*** ***hydrolase*** and its substrate under the same conditions as those under which an intermediate was shown for both microsomal and sol. ***epoxide*** ***hydrolases*** and therefore indicated that the cholesterol ***epoxide*** ***hydrolase*** apparently does not act by a similar mechanism and is probably not structurally related to microsomal and sol. ***epoxide*** ***hydrolases*** .

L19 ANSWER 26 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
1997:167263 Document No. 126:208769 Structure and mechanism of soluble ***epoxide*** ***hydrolase*** and its relation to microsomal ***epoxide*** ***hydrolase*** . ***Arand, Michael*** ; Hinz, Willy; Muller, Frank; Hanel, Karen; Winkler, Lars; Mecky, Astrid; Knehr, Michael; Durk, Heike; Wagner, Heike; et al. (Germany). Control Mechanisms of Carcinogenesis, 116-134. Editor(s): Hengstler, Jan Georg; Oesch, Franz. Institut fuer Toxikologie: Mainz, Germany. (English) 1996. CODEN: 64BFAM.
AB A review with 70 refs. ***Epoxide*** ***hydrolases*** are important safeguards of the organism against the potentially genotoxic and carcinogenic effects of epoxides. Recent advances in mol. cloning of sol. ***epoxide*** ***hydrolases*** have enhanced the understanding of the way in which these enzymes perform their catalytic task. Sequence similarity to a variety of bacterial enzymes, including haloalkane dehalogenases and bromoperoxidases among others, revealed the membership of ***epoxide*** ***hydrolases*** to the family of .alpha./.beta. hydrolase fold enzymes. A two-step enzymic mechanism for the ***epoxide*** ***hydrolases*** as implied by these findings could be proven by the trapping of an enzyme substrate ester intermediate formed in the first step of the catalytic reaction. Site-directed mutagenesis and biochem. characterization of the resp. mutants confirmed Asp333, His523 and Asp495 as the components of the catalytic triad of rat sEH that were predicted before by sequence alignments. Thus, the catalytic center of ***epoxide*** ***hydrolases*** is, in principle, well suited for the

processing of electrophilic substrates other than those carrying an epoxide structure. However, if these enzymes can really accept non-epoxide substrates remains to be elucidated.

L19 ANSWER 27 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
1996:630552 Document No. 125:269028 The catalytic activity of the endoplasmic reticulum-resident protein microsomal ***epoxide*** ***hydrolase*** towards carcinogens is retained on inversion of its membrane topology. Friedberg, Thomas; Holler, Romy; Loellmann, Bettina; ***Arand, Michael*** ; Oesch, Franz (Inst. Toxicol., Univ. Mainz, Mainz, D-55131, Germany). Biochemical Journal, 319(1), 131-136 (English) 1996. CODEN: BIJOAK. ISSN: 0264-6021. Publisher: Portland Press.
AB Diol epoxides formed by the sequential action of cytochrome P 450 and the microsomal ***epoxide*** ***hydrolase*** (mEH) in the endoplasmic reticulum (ER) represent an important class of ultimate carcinogenic metabolites of polycyclic arom. hydrocarbons. The role of the membrane orientation of cytochrome P 450 and mEH relative to each other in this catalytic cascade is not known. Cytochrome P 450 is known to have a type I topol. According to the algorithm of Hartman, Rapoport and Lodish (1989), which allows the prediction of the membrane topol. of proteins, mEH should adopt a type II membrane topol. Exptl., mEH membrane topol. has been disputed. This study demonstrates that, in contrast with the theor. prediction, rat mEH has exclusively a type I membrane topol. Moreover, this topol. can be inverted without affecting the catalytic activity of mEH. These conclusions are supported by the observation that two mEH constructs (mEHg1 and mEHg2), contg. engineered potential glycosylation sites at two sep. locations after the C-terminal site of the membrane anchor, were not glycosylated in fibroblasts. However, changing the net charge at the N-terminus of these engineered mEH proteins by +3 resulted in proteins (++mEHg1 and ++mEHg2) that became glycosylated and consequently had a type II topol. The sensitivity of these glycosylated proteins to endoglycosidase H indicated that, like the native mEH, they are still retained in the ER. The engineered mEH proteins were integrated into membranes as they were resistant to alk. extn. Interestingly, an insect mEH with a charge distribution in its N-terminus similar to ++mEHg1 has recently been isolated. This enzyme might well display a type II topol. instead of the type I topol. of the rat mEH. Importantly, mEHg1, having the natural cytosolic orientation, as well as ++mEHg1, having an artificial luminal orientation, displayed rather similar substrate turnovers for the mutagenic metabolite benzo[a]pyrene 4,5-oxide. To our knowledge this is the first report demonstrating that topol. inversion of a protein within the membrane of the ER has only a moderate effect on its enzymic activity, despite differences in folding pathways and redox environments on each side of the membrane. This observation represents an important step in the evaluation of the influence of mEH membrane orientation in the cascade of events leading to the formation of ultimate carcinogenic metabolites, and for studying the general importance of metabolic channeling on the surface of membranes.

L19 ANSWER 28 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
1996:515878 Document No. 125:215259 Investigating the role of the microsomal ***epoxide*** ***hydrolase*** membrane topology and its implication for drug metabolism pathways. Friedberg, Thomas; Loellmann, Bettina; Becker, Roger; Holler, Romy; ***Arand, Michael*** ; Oesch, Franz (Inst. Toxicol., Univ. Mainz, Mainz, D-55131, Germany). Advances in Experimental Medicine and Biology, 387(Biological Reactive Intermediates V), 17-24 (English) 1996. CODEN: AEMBAP. ISSN: 0065-2598. Publisher: Plenum.
AB A review with 21 refs. The microsomal ***epoxide*** ***hydrolase*** (mEH) catalyzes the hydrolysis of reactive epoxides which are formed by the action of cytochromes P 450 from xenobiotics. In addn. the mEH has been found to mediate the transport of bile acids. For the mEH it has been shown that it is cotranslationally inserted into the endoplasmic reticulum. We have demonstrated that the amino-terminal twenty amino acid residues of this protein serve as its single membrane anchor signal sequence and that the function of this sequence can be also supplied by a cytochrome P 450 (CYP2B1) anchor signal sequence. In addn. we present data showing that the membrane anchor signal sequence of the mEH is dispensable for the catalytic activity of this protein. Our results indicate that is might be feasible to invert the topol. of the mEH in the membrane of the endoplasmic reticulum without affecting the catalytic activity of this protein. With this strategy it will be possible to

investigate whether the membrane topol. of xenobiotic metabolizing enzymes is important for their role in chem. carcinogenesis.

L19 ANSWER 29 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
1996:130544 Document No. 124:197046 Asp333, Asp495, and His523 form the catalytic triad of rat soluble ***epoxide*** ***hydrolase*** . ***Arand, Michael*** ; Wagner, Heike; Oesch, Franz (Institute Toxicology, University Mainz, Mainz, D-55131, Germany). Journal of Biological Chemistry, 271(8), 4223-9 (English) 1996. CODEN: JBCHA3. ISSN: 0021-9258. Publisher: American Society for Biochemistry and Molecular Biology.

AB On the basis of the sequence similarity between mammalian ***epoxide*** ***hydrolases*** and bacterial haloalkane dehalogenase reported earlier, the authors selected candidate amino acid residues for the putative catalytic triad of rat sol. ***epoxide*** ***hydrolase*** (I). The predicted amino acid residues were exchanged by site-directed mutagenesis of I cDNA, followed by the expression of the resp. mutant enzymes in Escherichia coli. A total of 25 different mutants were analyzed for their I activity toward the model substrate, trans-stilbene oxide. In case of impaired catalytic activity of a given mutant, the structural integrity of the recombinant enzyme protein was assessed either by its ability to covalently bind trans-stilbene oxide or by affinity purifn. on benzyl thio-Sepharose, using the sol. I-specific competitive inhibitor, 4-fluorochalcone oxide, to release the bound enzyme from the affinity matrix. Of the mutants under investigation, only those with changes in positions Asp-333, Asp-495, and His-523 were completely inactive toward trans-stilbene oxide while retaining the proper protein fold. These amino acids were exactly those previously predicted by sequence alignment. Exchange of the amino acid residues flanking the catalytic nucleophile, Asp-333, significantly changed the kinetic properties of the enzyme. Mutation of His-332 to Gln had no apparent effect on the Km but led to a heavily reduced Vmax (5% of that of the wild-type enzyme) of mutant I, whereas the exchange of Trp-324 with Phe strongly increased the Km (7-fold) and also moderately enhanced the Vmax (2-fold) of the corresponding mutant. Mutation of Trp-540 apparently had a strong effect on protein conformation.

L19 ANSWER 30 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
1995:647095 Document No. 123:48103 Induction of rat liver microsomal ***epoxide*** ***hydrolase*** by its endogenous substrate 16.alpha.,17.alpha.-epoxyestra-1,3,5-trien-3-ol. Faendrich, F.; Degiuli, B.; Vogel-Bindel, U.; ***Arand, M.*** ; Oesch, F. (Institute of Toxicology, University of Mainz, Mainz, D-55131, Germany). Xenobiotica, 25(3), 239-44 (English) 1995. CODEN: XENOBH. ISSN: 0049-8254. Publisher: Taylor & Francis.

AB The influence of the endogenous steroid epoxides 16.alpha.,17.alpha.-epoxyestra-1,3,5(10)-trien-3-ol (estroxide) and 16.alpha.,17.alpha.-epoxiandrost-4-en-3-one (androstene oxide) and their metabolic precursors estra-1,3,5(10), 16-tetraen-3-ol (estratetraenol) and androsta-4,16-dien-3-one (androstadienone) on the specific activities of hepatic microsomal and sol. ***epoxide*** ***hydrolase*** , glutathione S-transferase, dihydrodiol dehydrogenase, and 7-ethoxycoumarin deethylase was investigated in the male Sprague-Dawley rat. Both estroxide and estratetraenol induced microsomal ***epoxide*** ***hydrolase*** activity towards styrene oxide and estroxide itself 2--2.5-fold and glutathione conjugation of 1-chloro-2,4-dinitrobenzene (CDNB) 1.6-fold after i.p. administration of a high dose of compd. (300 mg/kg). In addn., estroxide decreased 7-ethoxycoumarin deethylation down to 20% of the activity obsd. in the untreated rat, whereas estratetraenol enhanced the activity of sol. ***epoxide*** ***hydrolase*** towards trans-stilbene oxide by a factor of 1.7. In contrast, neither androstene oxide nor androstadienone showed a significant influence on any of the parameters under investigation. Dihydrodiol dehydrogenase was not significantly changed by any of the treatments.

L19 ANSWER 31 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
1995:334693 Document No. 122:283587 Gene evolution of ***epoxide*** ***hydrolases*** and recommended nomenclature. Beetham, Jeffrey K.; Grant, David; ***Arand, Michael*** ; Garbarino, Joan; Kiyosue, Tomohiro; Pinot, Franck; Oesch, Franz; Belknap, William R.; Shinozaki, Kazuo; Hammock, Bruce D. (Dep. Entomology and Environmental Toxicology,

Univ. Calif., Davis, CA, 95616, USA). DNA and Cell Biology, 14(1), 61-71 (English) 1995. CODEN: DCEBE8. ISSN: 1044-5498. Publisher: Liebert.

AB We have analyzed amino acid sequence relationships among sol. and microsomal ***epoxide*** ***hydrolases*** , haloacid dehalogenases, and haloalkane dehalogenase. The amino-terminal residues (1-229) of mammalian sol. ***epoxide*** ***hydrolase*** are homologs to a haloacid dehalogenase. The carboxy-terminal residues (230-554) of mammalian sol. ***epoxide*** ***hydrolase*** are homologs to haloalkane dehalogenase, to plant sol. ***epoxide*** ***hydrolase*** , and to microsomal ***epoxide*** ***hydrolase*** . The shared identity between the haloacid and haloalkane dehalogenases does not indicate relatedness between these two types of dehalogenases. The amino-terminal and carboxy-terminal homologies of mammalian sol. ***epoxide*** ***hydrolase*** to the resp. dehalogenases suggests that this ***epoxide*** ***hydrolase*** , but not the sol. ***epoxide*** ***hydrolase*** of plant or the microsomal ***epoxide*** ***hydrolase*** , derives from a gene fusion. The homol. of microsomal to sol. ***epoxide*** ***hydrolase*** suggests they derive from a gene duplication, probably of an ancestral bacterial (***epoxide***) ***hydrolase*** gene. Based on homol. to haloalkane dehalogenase, the catalytic residues for the sol. and microsomal ***epoxide*** ***hydrolases*** are predicted. A nomenclature system based on divergent mol. evolution is proposed for these ***epoxide*** ***hydrolases*** .

L19 ANSWER 32 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN

1995:317539 Document No. 122:75673 Xenobiotic metabolizing enzyme activities and viability are well preserved in EDTA-isolated rat liver parenchymal cells after cryopreservation. Diener, Bernd; Abdel-Latif, hassan; ***Arand, Michael*** ; Oesch, Franz (Inst. Toxicol., Univ. Mainz, Mainz, D-55131, Germany). Toxicology and Applied Pharmacology, 130(1), 149-53 (English) 1995. CODEN: TXAPA9. ISSN: 0041-008X. Publisher: Academic.

AB Rat liver parenchymal cells (PC) were isolated by EDTA perfusion and were purified by a subsequent Percoll centrifugation. The isolated PC had a viability of 95%, as judged by trypan blue exclusion. Freshly isolated PC were cryopreserved with an optimized protocol in a computer-controlled freezer. After thawing, the PC still retained a viability of 89%. The activities of representative xenobiotic metabolizing enzymes were compared between freshly isolated and cryopreserved PC after thawing. The cytochrome P 450 content and the cytochrome P 450 2C11 isoenzyme activity, detd. by hydroxylation of testosterone in intact cells, were not affected by the cryopreservation. The following phase II enzyme activities were also well maintained after cryopreservation: phenol sulfotransferase (92%), 1-naphthol UDP-glucuronosyl transferase (95%), sol. ***epoxide*** ***hydrolase*** (87%), and glutathione S-transferase (88%), detd. with broad spectrum substrate 1-chloro-2,4-dinitrobenzene. However, there was a significant decrease in plating efficiency between freshly isolated (86%) and cryopreserved (57%) PC when they were cultured. The initial quality of the freshly isolated PC is decisive for the success of cryopreservation. These results support the use of cryopreserved PC in pharmacol. and toxicol. with the aim to reduce the no. of exptl. animals used.

L19 ANSWER 33 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN

1995:258588 Document No. 122:48662 Xenobiotic metabolizing enzyme activities in isolated and cryopreserved human liver parenchymal cells. Diener, B.; Traiser, M.; ***Arand, M.*** ; Leissner, J.; Witsch, U.; Hohenfellner, R.; Faendrich, F.; Vogel, I.; Utesch, D.; Oesch, F. (Institute of Toxicology, University of Mainz, Obere, D-55131, Germany). Toxicology in Vitro, 8(6), 1161-6 (English) 1994. CODEN: TIVIEQ. ISSN: 0887-2333. Publisher: Elsevier.

AB Liver parenchymal cells (hepatocytes) of human organ donors were isolated using a two-step collagenase perfusion technique. The av. viability of the freshly isolated liver parenchymal cells, as judged by trypan blue exclusion, was 82%. The inter-individual differences in the detd. enzyme activities were less than a factor of 7.5, despite the different sexes and ages of the donors. Freshly isolated parenchymal cells (PC) were cryopreserved using a computer-controlled freezing protocol. After thawing, cryopreserved cells had a mean viability of 57%. The activities of xenobiotic metabolizing enzymes in freshly isolated and cryopreserved cells were compared using PC from two donors. The enzyme activities of

phenol sulfotransferase, 1-naphthol UDP-glucuronosyltransferase and microsomal ***epoxide*** ***hydrolase*** were well maintained after thawing (87-117% of activities in freshly isolated cells), whereas the activities of glutathione S-transferase, monitored with the broad spectrum substrate 1-chloro-2,4-dinitrobenzene, and the major broad spectrum cytosolic ***epoxide*** ***hydrolase*** were moderately but markedly reduced after cryopreservation (34-64% and 45-89% of levels in fresh cells, resp.). The decrease of both activities was dependent on the viability after thawing. When cryopreserved cells were purified by a Percoll centrifugation after thawing, the viability was increased from 62 to 92% for cells from one of the donors and from 88 to 98% for PC for the other donor. Subsequently the activity of glutathione S-transferase in Percoll-purified PC from the two donors was increased to 71 and 96% of levels in freshly isolated cells. It is concluded that the use of cryopreserved liver parenchymal cells of humans and other species represents a valuable tool in predicting which animal species best represents humans in hepatic metab. and therefore should be the preferred species for investigations of metab. and metab.-dependent toxicities.

L19 ANSWER 34 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
1995:220048 Document No. 123:3944 Enzymic epoxide hydration involves a hydroxyacyl intermediate. Lacourciere, G. M.; Armstrong, R. N.; Hammock, B. D.; Pinot, F.; Beetham, J. K.; Grant, D. F.; ***Arand, M. E.*** ; Oesch, F.; ***Arand, M.*** ; et al. (Stony Brook Campus, New York University, USA). Chemtracts: Organic Chemistry, 7(4), 247-51 (English) 1994. CODEN: CMOCEI. ISSN: 0895-4445. Publisher: Data Trace Chemistry Publishers.
AB The title research of G. M. Lacourciere, R. N. Armstrong, B. D. Hammock, F. Pinot, J. K. Beetham, D. F. Grant, M. E. Arand, F. Oesch, T. Freiberg, and M. Arand (1994) is reviewed with commentary and 6 refs.

L19 ANSWER 35 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
1994:238997 Document No. 120:238997 Isolation of a putative hydroxyacyl enzyme intermediate of an ***epoxide*** ***hydrolase*** . Hammock, Bruce D.; Pinot, Franck; Beetham, Jeffery K.; Grant, David F.; ***Arand,*** *** Michael E.*** ; Oesch, Franz (Dep. Entomol., Univ. California, Davis, CA, USA). Biochemical and Biophysical Research Communications, 198(3), 850-6 (English) 1994. CODEN: BBRCA9. ISSN: 0006-291X.
AB A putative covalent, .alpha.-hydroxyacyl intermediate was isolated by the brief exposure of murine sol. ***epoxide*** ***hydrolase*** to its substrate. The reaction was reversed by time and blocked by competitive inhibitors. The formation of the intermediate was dependent upon the concn. of the enzyme and was increased by incubation under acidic conditions. The structure of the intermediate was supported by microchem. methods.

L19 ANSWER 36 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
1994:186080 Document No. 120:186080 Sequence similarity of mammalian ***epoxide*** ***hydrolases*** to the bacterial haloalkane dehalogenase and other related proteins. Implication for the potential catalytic mechanism of enzymic epoxide hydrolysis. ***Arand, Michael*** ; Grant, David F.; Beetham, Jeffrey K.; Friedberg, Thomas; Oesch, Franz; Hammock, Bruce D. (Institute of Toxicology, University of Mainz, Obere Zahlbacherstr. 67, Mainz, D-55131, Germany). FEBS Letters, 338(3), 251-6 (English) 1994. CODEN: FEBLAL. ISSN: 0014-5793.
AB Direct comparison of the amino acid sequences of microsomal and sol. ***epoxide*** ***hydrolase*** superficially indicates that these enzymes are unrelated. Both proteins, however, share significant sequence similarity to a bacterial haloalkane dehalogenase that has earlier been shown to belong to the .alpha./.beta. hydrolase fold family of enzymes. The catalytic mechanism for the dehalogenase has been elucidated in detail [Verschueren et al. (1993) Nature 363, 693-698] and proceeds via an ester intermediate where the substrate is covalently bound to the enzyme. From these observations the authors conclude (i) that microsomal and sol. ***epoxide*** ***hydrolase*** are distantly related enzymes that have evolved from a common ancestral protein together with the haloalkane dehalogenase and a variety of other proteins specified in the present paper, (ii) that these enzymes most likely belong to the .alpha./.beta. hydrolase fold family of enzymes and (iii) that the enzymic epoxide hydrolysis proceeds via a hydroxy ester intermediate, in contrast to the presently favored base-catalyzed direct attack of the epoxide by an

activated water.

L19 ANSWER 37 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
1993:620402 Document No. 119:220402 Isolation and characterization of a cDNA encoding rat liver cytosolic ***epoxide*** ***hydrolase*** and its functional expression in Escherichia coli. Knehr, Michael; Thomas, Helmut; ***Arand, Michael*** ; Gebel, Thomas; Zeller, Hans Dieter; Oesch, Franz (Inst. Toxicol., Univ. Mainz, Mainz, W-6500, Germany). Journal of Biological Chemistry, 268(23), 17623-7 (English) 1993. CODEN: JBCHA3. ISSN: 0021-9258.
AB A cDNA of 1992 base pairs encoding the complete rat liver cytosolic ***epoxide*** ***hydrolase*** has been isolated using a polymerase chain reaction-derived DNA fragment (Arand, M., Knehr, M., Thomas, H., Zeller, H. D., and Oesch, F. (1991) FEBS Lett. 294, 19-22) known to represent the 3'-end of the cytosolic ***epoxide*** ***hydrolase*** mRNA. Sequence anal. revealed an open reading frame of 1662 nucleotides corresponding to 554 amino acids (Mr = 62,268). The DNA sequence obtained did not display significant homol. to the sequences of microsomal ***epoxide*** ***hydrolase*** or leukotriene A4 hydrolase or to any other DNA included in the EMBL Data Bank (release 32). On Northern blotting of rat liver RNA, a single mRNA species was detected that was strongly induced on treatment of the animal with fenofibrate, a potent peroxisome proliferator. The most significant structure of the deduced protein is a modified peroxisomal targeting signal (Ser-Lys-Ile) at the carboxyl terminus that is regarded to be responsible for the unusual dual localization of the cytosolic ***epoxide*** ***hydrolase*** in peroxisomes as well as in the cytosol. In addn., a leucine zipper-like motif was identified at the amino terminus. Its possible implication for the obsd. dimeric structure of cytosolic ***epoxide*** ***hydrolase*** is discussed. The isolated cDNA was expressed in bacteria to yield a catalytically active enzyme. Specific activity of the crude lysate obtained exceeded that of rat liver cytosols from maximally induced animals by a factor of 8.

L19 ANSWER 38 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
1993:596735 Document No. 119:196735 The use of the PCR technique in cloning low abundant genes: isolation of a cytosolic ***epoxide*** ***hydrolase*** cDNA. Knehr, Michael; ***Arand, Michael*** ; Hagen, Maria; Zeller, Hans Dieter; Thomas, Helmut; Oesch, Franz (Inst. Toxicol., Univ. Mainz, Mainz, D-6500, Germany). Eur. Biotechnol. Today, 217-22. Editor(s): Malvasi, Fabio; Cortese, Riccardo; Albertini, Alberto. Intercept: Andover, UK. (English) 1992. CODEN: 59HHAE.
AB In the authors lab. they are working on the characterization of drug metabolizing enzymes involved in the control of potentially mutagenic and/or carcinogenic intermediates of endogenous and exogenous compds. One of these enzymes, cytosolic ***epoxide*** ***hydrolase*** (cEH), detoxifies a variety of very electrophilic epoxides which can otherwise bind to proteins, RNA or DNA (Meijer and Depierre, 1988). Attempts to isolate a specific cDNA for cEH using either antibodies or oligonucleotides derived from parts of the underlying amino acid sequence did not lead to success. Applying those oligonucleotides as sense primers in PCR in combination with an oligo-dT primer resulted in the specific amplification of the 3'-end of the desired cDNA (Arand et al., 1991). Using the latter as a probe in screening a plasmid cDNA library, the authors isolated a full-length clone which is currently under investigation (in prepn.). The authors think this strategy should be applicable for any rare gene of interest if it is possible to design useful sense primers. Some facts concerning this point are discussed later in this paper. Addnl., the authors show an alternative strategy to obtain a full length clone, again using oligonucleotides as PCR primers.

L19 ANSWER 39 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
1993:121439 Document No. 118:121439 Xenobiotic-metabolizing enzyme activities in hybrid cell lines established by fusion of primary rat liver parenchymal cells with hepatoma cells. Utesch, D.; ***Arand, M.*** ; Thomas, H.; Petzinger, E.; Oesch, F. (Inst. Toxicol., Univ. Mainz, Mainz, D-6500, Germany). Xenobiotica, 22(12), 1451-7 (English) 1992. CODEN: XENOBH. ISSN: 0049-8254.
AB The activities of xenobiotic-metabolizing enzymes were detd. in hybrid cell lines (hepatocytoma, HPCT) that have been established by fusion of liver parenchymal cells from adult rat (PC) with cells from a Reuber

hepatoma cell line (FAO). Cytochrome P 450 was not measurable spectrophotometrically in FAO and HPCT. P 450-dependent conversion of testosterone was below the detection limit in FAO and only marginally present in HPCT. Microsomal and cytosolic ***epoxide*** ***hydrolase*** , glutathione S-transferase, and phenol sulfotranserase were low or even below detection limits in FAO. These enzyme activities were higher in HPCT and corresponded to .apprx.1-10% of the activities measured in PC. 1-Naphthol UDP-glucuronosyl transferase activity was .apprx.20% in FAO and .apprx.100% in HPCT compared to PC. Metabolic conversion of benzo[a]pyrene was low in FAO, high in PC, and intermediate in HPCT. The data, however, do not allow the conclusion of whether this intermediate rate is catalyzed by similar P 450 isoenzymes as in PC. Due to the easily measurable phase II-metabolizing enzyme activities HPCT may, however, be useful for in vitro enzyme induction or repression studies.

L19 ANSWER 40 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
1993:35037 Document No. 118:35037 An impaired peroxisomal targeting sequence leading to an unusual bicompartmental distribution of cytosolic ***epoxide*** ***hydrolase*** . ***Arand, Michael*** ; Knehr, Michael; Thomas, Helmut; Zeller, Hans Dieter; Oesch, Franc (Inst. Toxicol., Univ. Mainz, Mainz, D-6500, Germany). FEBS Letters, 294(1-2), 19-22 (English) 1991. CODEN: FEBLAL. ISSN: 0014-5793.
AB The C-terminal region of rat liver cytosolic ***epoxide*** ***hydrolase*** (cEH) was analyzed by means of cDNA cloning to define the structure of its possible peroxisomal targeting sequence (PTS). Purified cEH was subjected to peptide anal. following endoproteinase Glu-C digestion and HPLC-sepn. of the fragments. The obtained sequence information was used to perform PCR expts. resulting in the isolation of a 680-bp cDNA clone encoding the C-terminus of cEH. The deduced amino acid sequence displays a terminal tripeptide Ser-Lys-Ile which is highly homologous to the PTS (Ser-Lys-Leu) found in other peroxisomal enzymes. This slight difference appears to be sufficient to convert the signal sequence into an impaired and therefore ambivalent PTS, directing the enzyme partly to the peroxisomes and allowing part to reside in the cytosol.

L19 ANSWER 41 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
1989:449865 Document No. 111:49865 Rat liver cell type specific patterns of drug metabolizing enzymes and consequences for the control of genotoxic metabolites. Oesch, F.; Lafranconi, W. M.; ***Arand, M.*** ; Steinberg, P. (Inst. Toxicol., Univ. Mainz, Mainz, D-6500, Fed. Rep. Ger.). Microsomes Drug Oxid., Proc. Int. Symp., 7th, Meeting Date 1987, 346-53. Editor(s): Miners, J. O. Taylor & Francis: London, UK. (English) 1988. CODEN: 56NXA3.
AB In the rat liver, xenobiotic-metabolizing enzyme activities were consistently lower in the nonparenchymal cells than in the parenchymal cells (hepatocytes). Despite the normally low enzyme activities in nonparenchymal cells, these cells were capable of metabolizing some carcinogens to genotoxic species, which indicates that not only parenchymal cells but also nonparenchymal cells may contribute to the hepatic disposition and toxicity of xenobiotics.

L19 ANSWER 42 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
1987:434578 Document No. 107:34578 A time-course investigation of vitamin A levels and drug metabolizing enzyme activities in rats following a single treatment with prototypic polychlorinated biphenyls and DDT. Azais, Veronique; ***Arand, Michael*** ; Rauch, Petra; Schramm, Helga; Bellenand, Paul; Narbonne, Jean Francois; Oesch, Franz; Pascal, Gerard; Robertson, Larry W. (Lab. Sci. Consommation, INRA-CNRZ, Jouy-en-Josas, 78350, Fr.). Toxicology, 44(3), 341-54 (English) 1987. CODEN: TXCYAC. ISSN: 0300-483X.
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AB Xenobiotics previously characterized as selective inducers of drug-metabolizing enzymes were chosen to probe possible relations between

enzyme induction and vitamin A metab. Liver, kidney, and serum retinol and retinyl palmitate levels were investigated in male rats receiving a single i.p. injection of the PCBs, 2,2',5,5'-tetrachlorobiphenyl (I), 3,3',4,4'-tetrachlorobiphenyl, or 2,2',4,4',5,5'-hexachlorobiphenyl (300 .mu.mol/kg). Whereas I, a weak or noninducer, and 2,2',4,4',5,5'-hexachlorobiphenyl and DDT, phenobarbitol-type inducers of cytochrome P 450, led to no redn. in total vitamin A content of liver or kidney during the 7 day time-course, administration of 3,3',4,4'-tetrachlorobiphenyl, a toxic PCB and a potent 3-methylcholanthrene-type inducer of cytochrome P 450, resulted in progressively lowered liver vitamin A levels (to 40% of control values by day 7). During this time, kidney total vitamin A content increased 3-fold. The increase in kidney vitamin A (due primarily to increased retinol content) was only equal to 1/40 of total vitamin A which had disappeared from the liver. Although 3,3',4,4'-tetrachlorobiphenyl specifically induced certain drug-metabolizing enzyme activities, e.g. aryl hydrocarbon hydroxylase and UDP-glucuronosyltransferase (toward 4-nitrophenol), no highly significant correlations were found among the vitamin A levels and drug-metabolizing enzyme activities in the liver (aminopyrine N-demethylase, aryl hydrocarbon hydroxylase, aldrin epoxidase, microsomal ***epoxide*** ***hydrolase*** , UDP-glucuronosyltransferase toward 4-nitrophenol, glutathione transferase toward 1-chloro-2,4-dinitrobenzene, and cytochrome P 450 content) as detd. by multiple linear regression anal.

L19 ANSWER 43 OF 43 CAPLUS COPYRIGHT 2004 ACS on STN
1987:114957 Document No. 106:114957 Cis- and trans-1,2-diphenylaziridines: induction of xenobiotic-metabolizing enzymes in rat liver and mutagenicity in Salmonella typhimurium. Glatt, H. R.; Robertson, L. W.; ***Arand,*** *** M.*** ; Rauch, P.; Schramm, H.; Setiabudi, F.; Poechlauer, P.; Mueller, E. P.; Oesch, F. (Inst. Toxicol., Univ. Mainz, Mainz, D-6500, Fed. Rep. Ger.). Archives of Toxicology, 59(4), 242-8 (English) 1986. CODEN: ARTODN. ISSN: 0340-5761.
GI

/ Structure 5 in file .gra /

AB The i.p. administration of trans-stilbene imine (I) [25125-72-8] resulted in statistically significant increases in the activities of aminopyrine N-demethylase [9037-69-8], microsomal ***epoxide*** ***hydrolase*** [***9048-63-9***], glutathione transferase [50812-37-8] (toward 1-chloro-2,4-dinitrobenzene, 1,2-dichloro-4-nitrobenzene, and .DELTA.5-androstene-3,17-dione) and UDP-glucuronosyltransferase [9030-08-4] (toward testosterone). cis-Stilbene imine [1605-06-7] was less potent in inducing these activities. Although I (total dose = 400 mg/kg) was more potent than trans-stilbene oxide [1439-07-2] (total dose = 1200 mg/kg) in inducing the activities of glutathione transferase and UDP-glucuronosyltransferase both compds. belong to the class of substances which are more potent inducers of conjugating (phase II) enzymes. Because of their structural similarity with K-region arene imines which are potent mutagens, cis-stilbene imine and I were investigated for mutagenicity (reversion of his- strains of S. typhimurium). cis-Stilbene imine and I were direct mutagens in the strain TA100. This result, and the finding that acenaphthene 1,2-imine [7156-07-2] efficiently reverts various strains of S. typhimurium, demonstrates that not only K-region arene imines, but also other aziridines substituted at the 2 C atoms with arom. moieties, are mutagenic.

	L #	Hits	Search Text	DBs
1	L1	376	EPOXIDE ADJ HYDROLASE	USPAT ; US-PG PUB
2	L2	16820	ASPERGILLUS	USPAT ; US-PG PUB
3	L3	66037	FUNGUS OR FUNGAL	USPAT ; US-PG PUB
4	L4	116	L1 AND L2	USPAT ; US-PG PUB
5	L5	4	L1 NEAR6 L2	USPAT ; US-PG PUB
6	L6	6	L1 NEAR10 L2	USPAT ; US-PG PUB
7	L7	26	L1 NEAR15 L3	USPAT ; US-PG PUB
8	L8	21	L7 NOT L6	USPAT ; US-PG PUB
9	L9	27	L6 OR L8	USPAT ; US-PG PUB